HAZARDOUS CONTAMINANTS PROGRAMME

ENVIRONMENTAL ASPECTS OF SELECTED AROMATIC AMINES AND AZO DYES IN ONTARIO

REPORT No. ARB-TDA-83-79

AUGUST 1980

Ministry of the Environment
Ontario

The Honourable
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Minister

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Deputy Minister

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Prepared For

Air Resources Branch
Ontario Ministry of the Environment

By

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August, 1980

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CONCLUSIONS AND RECOMMENDATIONS

The study which provided the basis for this report was commissioned by the Ontario Ministry of the Environment as part of their ongoing environmental risk assessment program.

The report presents a state of the art summary and review of the generally available scientific and technical information on aromatic amines and azo dyes. This information was obtained by means of literature searches and supplemented by discussions with knowledgeable sources in the university, government and industrial communities.

In general, it was noted that data specific to emissions in Ontario were lacking, as were data qualifying ambient environmental concentrations.

In Ontario, there is no primary manufacturing of either aromatic amines or azo dyes. Consequently, the hazards and emissions associated with these processes are absent and not of concern.

However, the primary aromatic amines, particularly aniline, are feedstocks for the rubber chemicals industry. In this industry they are subjected to reactions which produce various substituted aromatic amines. The products are ultimately consumed by the rubber compounding industry.

There are several other consumers of aromatic amines in Ontario, such as the agricultural chemicals industry and pharmaceutical-cosmetics industries, but their rates of consumption seem small in comparison to the rubber industry.

Dyes, specifically including azo types, are consumed in large quantities, primarily by the pulp and paper and textile industries. Numerous smaller consumers exist but their total consumption is small when compared to that of the two industries mentioned.

Aromatic amines in general are considered toxic and many of them are considered carcinogens in animals. Presently, only five aromatic amines are recognized as carcinogenic in humans, where they produce papillomas and cancer of the urinary bladder. These five are: benzidine, 4-aminobiphenyl, auramine, beta-naphthylamine and N,N-bis(2-chloroethyl)-2-napththylamine.

A large number of azo compounds have been found to be carcinogenic in animals. However, no cases of human cancer have, as yet, been attributed to any specific aromatic azo compound.

Both aromatic amines and azo dyes are known to react with chlorine, ozone and light; but the data suggest that these reactions, in the environmental context, do not result in ultimate degradation. Both groups of compounds have demonstrated a high degree of resistance to biodegradation, and azo dyes are considered toxic to common micro-organisms.

Information relating to the discharge of both aromatic amines and azo dyes is scarce and equivocal.

In order to define the magnitude of the risk to health and the environment stemming from the use of these compounds, it is recommended that a detailed program of study be considered.

Specifically, it is suggested that the major user industries identified in this report be examined in detail. The objective should be the precise definition of the quanitities and qualities of related wastes discharged from their operations.

No information which defines the ambient environmental concentrations of either aromatic amines or azo dyes in Ontario or elsewhere was identified. In consideration of their demonstrated toxicity, this is a definite data shortfall.

Accordingly, it is recommended that the Ontario Ministry of the Environment consider the initiation of a monitoring study with the objective of defining the ambient environmental concentrations of aromatic amines and azo dyes in Ontario.

This study should be preceded by and correlated to emission inventories to maximize information on local variations and general ambient concentrations.

This dual program of source study and monitoring could also provide useful data on environmental persistance. If significant environmental concentrations of either group of compounds is detected, a specific program to investigate their environmental degradation would be appropriate. Similarly, the toxicity of the intermediate products could be examined.

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INTRODUCTION 1

This study was commissioned by the Ontario Ministry of the Environment, as a part of their on-going environmental risk assessment programme.

The purpose of this report is to provide a state of the art summary and review of current scientific and technical information on the hazard posed by aromatic amines and azo dyes in Ontario.

The preliminary chapter presents general background information in terms of chemical, physical and industrial usage. This is followed by a chapter dealing with the toxicology of amines and azo compounds.

These chapters prepare the groundwork for the subsequent sections which examine aromatic amines and azo dyes with respect to several environmental depletion agents.

The most important industries and their effluents are discussed in the context of their discharges into the Ontario environment.

Since there is a distinct lack of specific information detailing environmental degradation pathways and the qualities of effluents discharged from industrial operations, it is felt that this approach provides a good perspective.

The theoretical background has been provided to allow reasonable judgements to be made where specific data is lacking.

BACKGROUND 2

2.1 AROMATIC AMINES

2.1.1 Introduction

Aromatic amines are defined as those in which an aromatic group is bonded directly to the nitrogen atom of the amino group. The simplest aromatic amine is Aniline, a compound ubiquitous in organic synthesis. Many simple aromatic amines are classified as derivatives of this basic molecule.

This investigation has examined the usage of the materials illustrated in Fig. 2.1.1, and it is suggested the reader periodically refer to these illustrations.

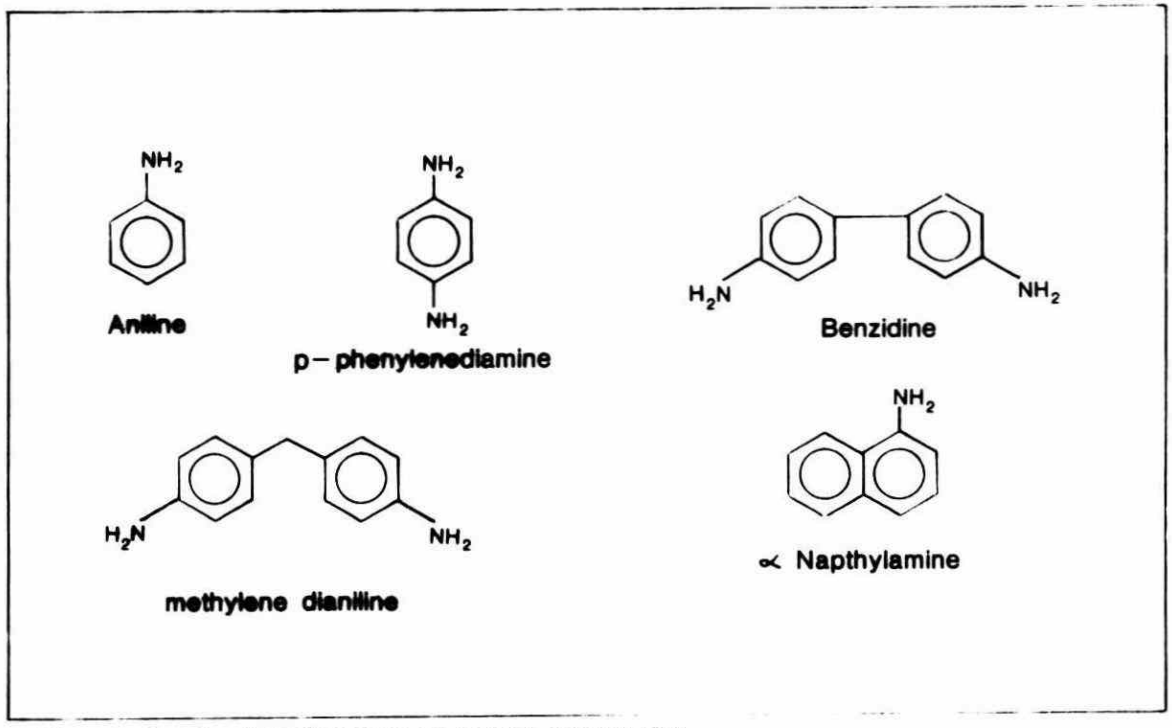


Figure 2.1.1 "PRIMARY GROUP AMINES"

TABLE 2.1.1

GENERAL USES OF "PRIMARY GROUP AMINES"

Anilines	used in synthesis of:	diphenylamine
	:	hydroquinone
	:	dye manufacture
	:	photochemicals
	:	isocyanates
	:	explosives
	:	pesticides
	:	herbicides
	:	pharmaceuticals
	:	synthetic sweeteners
	:	rubber chemicals
	:	plasticizers
	used as:	corrosion inhibitors
	:	surfactants
	:	catalysts
	:	as hardener in epoxy resins
Phenylenediamines - meta	used in:	dye synthesis
	:	hair dyes
	:	hardener in epoxy resins
	:	high temperature polyamide resins
	:	isocyanates
- para	used in:	hair dyes
	:	photographic developer
	:	light sensitive lithography plates
	:	antioxidants
Benzidines	used in:	organic synthesis
	:	pharmaceuticals
	:	dye manufacture
	:	analytical reagent
	:	rubber compounding agent
	:	chemical analysis
Methylenedianilines	used in:	polyamide resins
	:	dye manufacture
	:	hardener in epoxy resins
	:	corrosion inhibition
	:	isocyanate synthesis
	:	chemical analysis
Naphthylamines	used in:	dye manufacturing
	:	herbicides
	:	antioxidants
	:	chemical analysis

Like ammonia, amines are polar compounds, and except for tertiary amines, can form intermolecular hydrogen bonds. Consequently, they have higher boiling points than non-polar compounds of the same molecular weight. However, their boiling points are below those of similar alcohols or carboxylic acids.

Most amines are capable of forming hydrogen bonds with water. As a result, the smaller amines exhibit water solubility, the borderline being reached at about six carbon atoms. Generally, simple amines do show solubility in less polar solvents such as ether, alcohol, benzene, etc.

The unsubstituted aromatic monoamines, except aniline, are only slightly soluble in water, the diamines show higher solubility.

Aromatic amines are very easily oxidized by air, and although most are colourless when pure, they are often discoloured by oxidation products. This property has been used advantageously in antioxidants.

Aromatic amines as distinct entities appear in many chemical process industries. However, their use in quantity is restricted to only a few. In this study, efforts have been concentrated on investigating areas in which there is the likelihood of broad population or environmental exposure, in significant concentration. Consequently, emphasis was placed on defining the usage of five aromatic amines: Aniline, phenylenediamine, benzidine, methylenedianiline and napthylamine. Their structures are illustrated in Fig. 2.1.1. This group of amines is referred to as "primary group amines".

2.1.2 Uses and Properties of Primary Group Amines

Table 2.1.1 lists general applications of the primary group amines. This information is general and does not necessarily relate to usage in Canada or specifically to Ontario.

Anilines

Important primary aromatic amines of this series include aniline, the toluidines, xylidines, and anisidines. The majority of these compounds are formed by the reduction of nitro compounds which can be synthesized by direct nitration of aromatics. They are solids or liquids of high boiling point and readily form characteristic derivatives. The majority of aromatic bases turn brown on exposure to light and air. Aniline, when pure, is a colorless oil with a bluish fluorescence.

The two most important uses of aniline are in the manufacture of dyes and rubber chemicals. The Colour Index lists 163 dyes made from aniline, and many others from aniline derivatives.

Aniline derivatives are used to a great extent in the rubber industry, which consumes most of the aniline imported into Canada. The derivatives are used as vulcanization accelerators and antioxidants. The accelerators include mercaptobenzothiazole and other thiazole derivatives, quanidine, and aniline-aldehyde condensates. Among rubber antioxidants are N-phenyl-2-naphthylamine and derivatives of diphenylamine and cyclohexylamine. N-Phenyl-1-naphthylamine is also used as a rubber antioxidant.

In the pharmaceutical industry, aniline is important in the manufacture of sulfa drugs and synthetic sweetening agents. The latter are derived from cyclohexylamine or from m-nitroaniline. Arsanilic acid, a growth stimulant for animals, is also of some importance.

Hydroquinone, derived from aniline, is important as a photographic chemical and intermediate for the preparation of antioxidants.

Resins from aniline and aldehydes, such as formaldehyde and furfural, have had some importance in the past.

Aniline has some importance as a corrosion inhibitor. It appears to be especially suitable for protecting some metals against wet carbon tetrachloride. Aniline phosphate is said to decrease the rate of corrosion of iron by seawater. Aniline may also be used in the production of epoxy and various other types of resins. Adducts of aniline with boron trifluoride, or condensation products with aldehydes, may be used as catalysts or curing agents for epoxy resins.

Various salts and reaction products of aniline have been suggested as additives for gasoline and lubricating oils and for use in various refining operations. Other products or mixtures may be used as rocket propellants.

Minor amounts of aniline and its derivatives are used in the textile, paper, and metallurgical industries; in the preparation of surfactants; as catalysts and stabilizers.

Phenylenediamines

Phenylenediamines occur as the ortho, meta and para isomers. All three are commonly obtained by the reduction of the dinitrobenzene and nitroaniline analogues.

In the pure form they are colourless solids which discolour rapidly in air.

o-Phenylenediamine is an important identification agent in analytical chemistry: for 1,2-diketones by the formation of quinoxalines; for carboxylic acids by the formation of 2-alkylbenz-imidazoles; and for the aliphatic or aromatic aldehydes by the formation of benzimidazoles. N-Phenyl-o-phenylenediamine is used in the preparation of some dyes, for example, the flavindulins.

Because of their ability to tetrazotize as well as to couple, m-phenylenediamine and toluene-2,4-diamine find their greatest value in the synthesis of azo dyes.

p-Phenylenediamines, especially the aryl derivatives, are also important dye intermediates.

The p-phenylenediamines are used extensively in photography. p-Phenylenediamine itself is a slow developing agent giving fine-grain results. The N,N-dialkyl-p-phenylenediamines are also fine-grain developers for black-and-white photography, but greater use is made of the ability of their oxidation products to react with active methylene compounds or phenols to give dyes in color photography. The diazonium compounds prepared from pheylenediamines, because of their photosensitivity, are used in diazo-type processes of photography.

p-Phenylenediamines are important antioxidants. In light-coloured synthetic or natural rubber compositions, N-aryl-p-phenylenediamines, such as N,N'-diphenyl-p-phenylenediamine and N,N'-di-2-naphthyl-p-phenylenediamine, which are almost free of staining, are used in large amounts.

Oxidation products of o-,m-,and p-phenylenediamines and of toluene-2,4-diamine have been used extensively in dyeing hair and fur.

Benzidines

Benzidine is the main product isolated in the rearrangement of hydrazobenzene, as white crystals, which darken in air. Benzidine is reported to be a mixture of three isotropic forms co-existing indefinitely at room temperature.

Benzidine, its homologous tolidines, and other derivatives of p,p'-diaminobiphenyl are of considerable importance as organic intermediates.

In inorganic qualitative and quantitative analysis, it is used for the determination of various cations and anions, in various phases of organic analyses, in the determination of blood in forensic and clinical medicine, and as stains in microscopy.

The major use of these compounds is as intermediates in the production of direct azo dyes. Several derivatives (e.g., o-tolidine, o-dianisidine, and 3,3'-dichlorobezidine) are also important pigment intermediates.

According to The Colour Index, 253 dyes based on benzidine have been reported.

Although a wide variety of p,p'-diaminobiphenyl derivatives are reported in the chemical literature, including nitrated, halogenated, sulfonated, carboxylated, acylated, and C-and N-alkylated derivatives, they are mainly of academic interest. However, the simple substituted compounds have been used commercially in the dye industry.

Methylenedianilines

In the pure form, methylenedianiline is a white crystal which rapidly discolours on exposure to air.

The most important isomer is the 4,4' derivative. This compound is commonly derived as a condensation product of aniline and formaldehyde. Alternatively, it may be obtained by the reduction of p,p-diaminobenzophenone.

The most important application of these materials is in the synthesis of dyestuffs, but some use as an epoxy resin hardening agent is reported.

Naphthylamines

Both the alpha and beta isomers of naphthylamine are white crystalline solids in the pure form but are rapidly discoloured on exposure to air.

Both isomers can be produced by the reduction of the appropriate nitro analogue, but beta-napthylamine is most commonly produced by the direct amination of beta-napthol.

Naphthylamines and their derivatives are of particular importance in the manufacture of azo dyestuffs and rubber chemicals.

A vapour phase condensation of alpha-naphthylamine with aniline yields N-phenyl-1-naphthylamine which is a rubber antioxidant and an important dye precursor.

Some use of alpha-naphthylamine has been made in the manufacture of rodenticides.

2.2 DYESTUFFS

2.2.1 Introduction

A dye can be defined as any substance which, when added in small quantities to another, causes a noticeable colouration.

A coloured organic compound is normally a highly unsaturated aromatic molecule containing an extensive conjugated linkage system.

The aromatic grouping is normally termed "the Chromogen". However, the actual colouration is due to the effect of substituent functionalities.

The "active" portions of a dye molecule are distinct structural features and can be grouped into three categories:

(a) the chromophore
(b) the auxochromes
(c) the linkage system

The chromophores are normally electron-withdrawing groups such as nitroso, azo or carbonyl. A selection of the more common chromophores is illustrated in Figure 2.2.1.

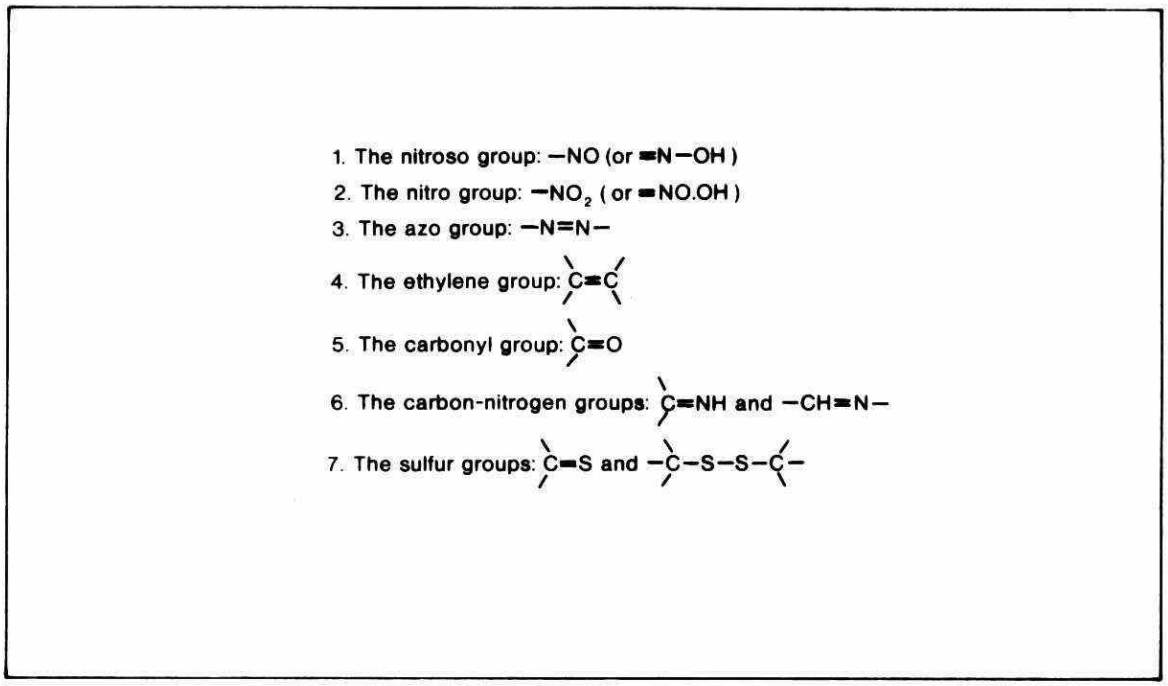


Figure 2.2.1 ILLUSTRATION OF COMMON CHROMOPHORES

In many cases, the dye may have some difficulty in attaching itself to the substrate. In order to alleviate this difficulty, the auxochromes are added. Their major function is to provide bonding capability. Normally, auxochromes are electron-releasing, salt forming functionalities such as amino or sulfonic acid groups.

Through the delocalized linkage system, both the chromophores and the auxochromes contribute to the formation of perceived colour. Colouration is achieved by shifting the absorption bands of the aromatic group to wavelengths in the visible region.

Generally, the dyes of commercial importance are based on a small group of aromatic systems. By varying the chromophores and their location within the molecule, the perceived colour is changed.

This method of colour production is reflected in one system of dye classification which groups dyes as derivatives of a given aromatic group i.e. cyanine dyes, anthraquinones, nitrodiarylamines.

Dyes are available in colours which exhibit variations in intensity. For example, a given shade of red may be either "dull" or "bright". If a dye has strong selective absorption, that is, if the absorption bands are narrow and rising steeply to high intensities, then it will be perceived as having a bright colour. Conversely, if the absorption bands are broad and of low intensity then the colour will be perceived as dull. An illustration of this is provided graphically in Figure 2.2.2.

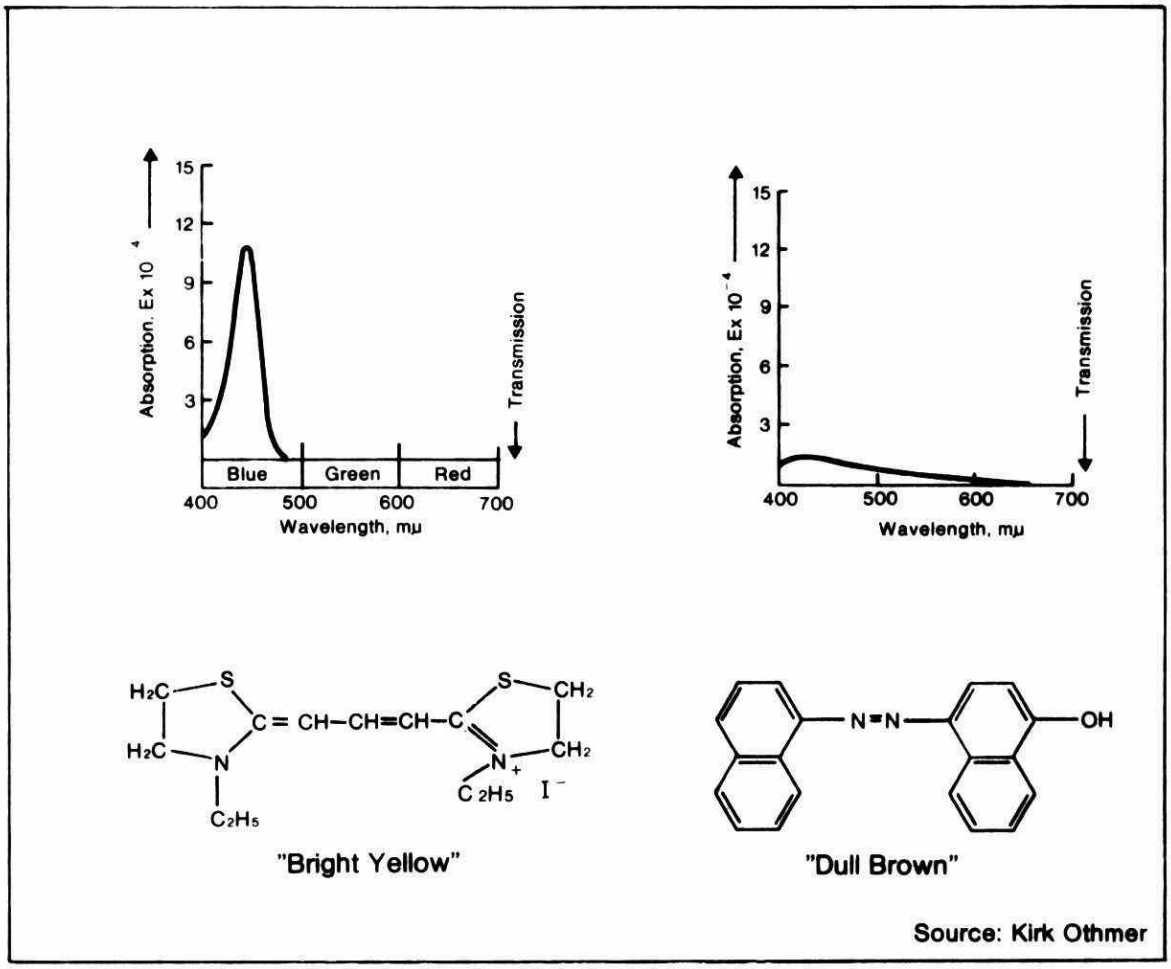


Figure 2.2.2 ILLUSTRATION OF THE ABSORPTION CURVES OF "BRIGHT" AND "DULL" DYES

This concept has commercial importance in terms of quantities required. If all other factors are equal, a dye which has a higher absorption will require quantitatively less dye. This colouring property is usually referred to in terms of "the extinction coefficient".

2.2.2 Classification of Dyes

Dyes are normally classified by either molecular structure or end use. The producers base their system on the molecular structure since many dyes differ simply by variations in chromophores.

However, the more common classification of dyes is according to their end use and method of application. This is the method adopted by most governments for publication of statistics and by "The Colour Index", which is the basic reference book for the dyestuffs industry. This method of classification has been adopted in this report.

The stress in this section is on the classes of dyes important in Ontario; it is not meant to represent a dye grouping's overall importance, nor does it describe all classes of dyes.

The most important classes in Ontario are: disperse, acid, basic, direct and solvent dyes. Each of these classes is discussed individually below.

Disperse Dyes

This class of dyes were variously known as acetate dyes, dispersed acetate dyes, dispersion dyes and dispersol dyes. The present universally accepted name, disperse dyes, was introduced in 1951. It is currently defined as "substantially water-insoluble dyes having specificity for one or more hydrophobic fibres, for example cellulose acetate and usually applied from fine aqueous dispersion".

Almost all disperse dyes are primary, secondary or tertiary amines of three main types; (a) aminoazobenzenes, (b) aminoanthraquinones and (c) nitrodiarylamines. These dyes do not contain solubilizing sulphonic acid groups.

Although substantially insoluble, these dyes are slightly soluble in water and uptake by the fibre is believed to take place from this aqueous phase. The degree of solubility influences the dyeing and levelling properties of the dye. The solubility of the dye and hence its equilibrium uptake and dyeing rate may be modified by the dispersing agent employed.

Dyes containing primary amino groups may be diazotised and developed on the fibre to produce dyeing of varying fastness according to the developers used. This procedure is widely used in the production of blacks.

These dyes find their greatest use in colouring of synthetic fibres such as acetate, triacetate, nylon and polyester; with the major material being polyester.

Acid Dyes

The acid dyes were probably originally so named because of the presence in their molecules of one or more sulphonic acid or other acidic groups. The term now applies to an application class rather than a chemical class. Since acidic groups are also present in many mordant, direct and reactive dyes their presence is not a distinguishing feature. Acid dyes are water-soluble anionic dyes that are applied to nitrogenous fibres such as wool, silk, nylon and modified acrylic fibres from acid or neutral baths. Attachment to the fibre is attributed, at least partly, to salt formation between anionic groups in the dyes and cationic groups in the fibre. Acid dyes are not substantive to cellulosic fibres.

Chemically the acid dyes consist of azo, anthraquinone, triphenylmethane, azine, xanthene, ketonimine, nitro and nitroso compounds. Azo dyes may be applied as pre-formed 1:1 or 1:2 metal complexes. A complete range of hues can be obtained, many of them being very bright, and the fastness properties vary from poor to very good.

Acid dyes are also applied by direct printing on protein fibres and nylon; selected dyes may be printed on viscose from a paste containing urea. Other important uses include the dyeing of leather, paper, jute, straw and anodised aluminum, the colouring of food and drink, drugs, cosmetics, insecticides, fertilizers, wood stains, varnishes, inks, plastics and resins, and the manufacture of toners and pigments of the lake type.

Basic Dyes

Basic dyes share the common characteristic of forming a coloured cation in aqueous solution.

Structurally, they are mainly from the triarylmethane or xanthene classes.

These dyes are used in the textile industry mainly to dye acrylic fibres, however, some use of them is made in dyeing silk, wool and cotton.

The paper industry uses large weights of the older basic dyes mainly for dyeing papers made from unbleached and mechanical pulps, or when light fastness is of little consequence. High lignin-content pulps have high substantivity for basic dyes, although this is reduced on bleaching. The solubility of basic dyes is not great, and solution problems are minimized by many dyes being available in liquid form.

Other uses are in the production of pigments and as solvent dyes and in the dyeing of leather; they appear in typewriter ribbons, carbon papers and duplicating inks.

Direct Dyes

The dyes within this section are those which were originally designed and marketed for the primary purpose of dyeing cotton. They are defined as "Anionic dyes substantive to cellulose when applied from an aqueous bath containing an electrolyte". They provide the simplest means of colouring cellulosic materials.

The majority of direct dyes belong to the di-, tris- and polyazo classes, the remainder being monoazo, stilbene, oxazine, thiazole and phthalocyanine compounds.

Some direct dyes have extensive use other than on cellulose fibres, many being of outstanding importance for use on paper, leather, wool, silk, nylon, bast fibres and for many miscellaneous purposes such as preparation of heavy-metal salts for use as pigments, biological stains, indicators, etc.

To be effective, direct dyestuffs must be long molecules, and the aromatic rings must be capable of assuming a co-planar configuration. Benzidine is commonly used as the basic "building block" since it allows the ideal spacing for the azo groups and is conducive to the desirable co-planar configuration.

Solvent Dyes

Solubility in an organic solvent (or solvents) is a characteristic physical property of a solvent dye. There are, however, important applications in which the solvent dye is incorporated directly into the product to be coloured.

Commercial solvent dyes are drawn from a number of chemical groups. Among the yellow, orange, brown and red hues, azo dyes predominate but xanthene dyes provide important bright red shades. The violet dyes are provided from the azo, anthraquinone, xanthene and triarylmethane groups. Among the more bathochromic hues, however, azo dyes have few representatives and the blue and green solvent dyes are predominantly of the anthraquinone and triarylmethane groups supported by examples from the azine, thiazine and phthalocyanine groups. Blacks are provided by the very important azine dye Nigrosine supported by a number of azo dyes. There are many dyes of unrecorded chemical constitution.

Solvent dyes are used for a great variety of purposes and new uses are constantly being found as new materials are brought into manufacture. The following, however, are the principal established uses:

- Spirit and oil wood stains and varnishes.

- Transparent lacquers incorporating nitrocellulose, cellulose acetate, vinyl, alkyd or other synthetic resins or shellac. These are used for many purposes including foil printing.

- Inks, for rotogravure and rubber stereo printing; for coating copying paper and typewriter ribbons; for ball point pens, and in printing inks as shading and brightening agents and for double tone effects.

- In fats, oils and waxes of all kinds for candles, sealing waxes, polishes, and surface finishes for a great variety of materials. For mass colouration of moulding powders and other constructional materials of cellulose acetate, celluloid, polystyrene, polymethacrylates, polyvinylchloride, phenol formaldehyde, urea formaldehyde, aminoplastics or other synthetic polymer compositions.

- In the leather industry for production of 'aniline' and 'semi-aniline' upper leathers and for spray finishing of dyed or undyed suede tannages. They are also used to correct off-shade dyeings by spraying from either solvent solution or aqueous/organic solvent emulsions. Solvent dyes are also used for paddle dyeing of furs and wool-skins.

Considerable interest has recently been shown in the use of solvent soluble dyes for dyeing of textiles, employing new techniques.

The chlorinated hydrocarbon solvents have attracted most attention for this particular application.

Some minor or specialised uses include the colouring of soap, cosmetics, gasoline and fuel oils and signalling smokes.

Miscellaneous

There are, in addition to those mentioned above, a considerable number of other dye classifications, most based on application.

However, in Ontario they appear to be of minor commercial significance and are therefore not discussed.

2.2.3 Synthesis of Azo Dyes

The characteristic feature of the azo colouring matters is the presence of the azo linkage as a chromophore. This chromophore is usually associated with auxochromic hydroxyl or amino groups.

Azo dyes are manufactured almost without exception by forming the diazonium salt of an aromatic amine which is then coupled to another aromatic compound. This coupling group can be another aromatic amine, a hydroxyl compound or a ketone capable of enolisation.

The two processes of diazotization and coupling are illustrated in Figure 2.2.3 using the simplest example of aniline and phenol to form p-hydroxyazobenzene.

The ease of diazotization depends markedly on the basicity of the amine. Extremely weak basic amines are diazotizable only by special methods.

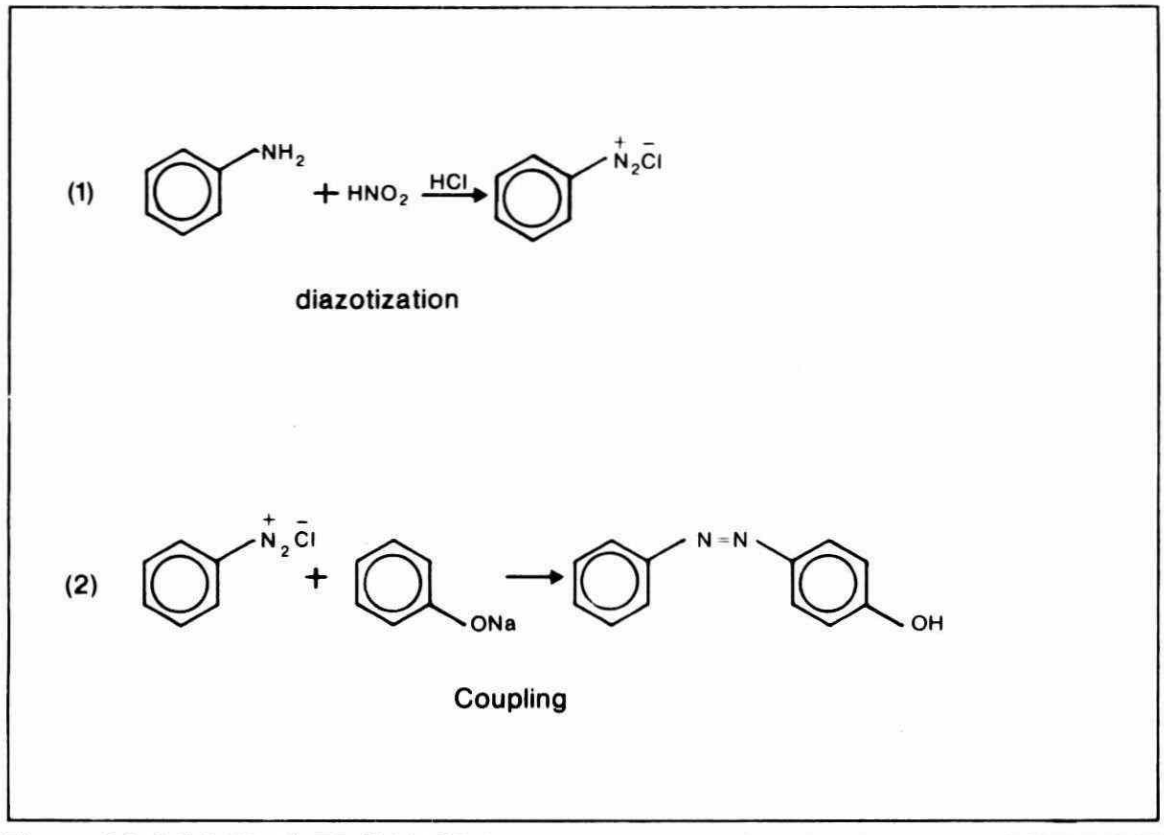


Figure2.2.3 SIMPLIFIED ILLUSTRATION OF DIAZOTIZATION AND COUPLING

The simple processes of diazotisation and coupling are applicable to a great number and variety of compounds including certain azo compounds which can themselves be diazotised or coupled. This enables the synthesis of "diazo" and "polyazo" dyes of various patterns. In consequence the azo dyes form by far the largest single class of synthetic dyes and have the widest range of applications: there are azo dyes for every fibre, natural and synthetic, for pigments and solvents and for a variety of minor non-textile applications.

2.2.4 Group Characteristics of Azo Dyes

Azo dyes are divided, according to the number and arrangement of azo groups present, into sub-classes conveniently designated by general formulae.

These formulae are normally in the form of letters indicating specific molecular groups and their relationships to each other.

In Table 2.2.1, we have excerpted from The Colour Index (P. 4009 ff), the general formulae and the chart describing the structural relationships in monazo, diazo and trisazo dyes.

The dyes can be separated into subgroups depending on whether or not they are water soluble. The water soluble dyes generally contain carboxylic acids, sulphonic acids or salt forming sulfonamide groups, whereas those lacking such groups are generally insoluble in water.

As illustrated in Table 2.2.1, it is clear that the vast majority of significant azo dyes belong to one or other of the subsections of each major grouping. Consequently, there are only about ten major classes of azo dyes.

The higher polyazo dyes (those of four azo linkages or more) are not of great commercial significance and are generally synthesized for specialty need. The synthetic principles of the major classes still apply to this group.

Figure 2.2.4 illustrates the use of Table 2.2.1 in structural analysis. One example has been selected for each of monazo, diazo and trisazo dyes. This is more generally illustrated in Figure 2.2.5 which shows the interrelationships between various starting materials and some dyes from each of the major classes.

From this it is clear that most dyes can be conveniently grouped by molecular structure. The colour variations are achieved simply by variation of the chromophore or auxochrome. For example in Figure 2.2.6, it can be seen that by adding an amino group to the basic structure of Solvent Yellow 2, Disperse Black 3 is obtained.

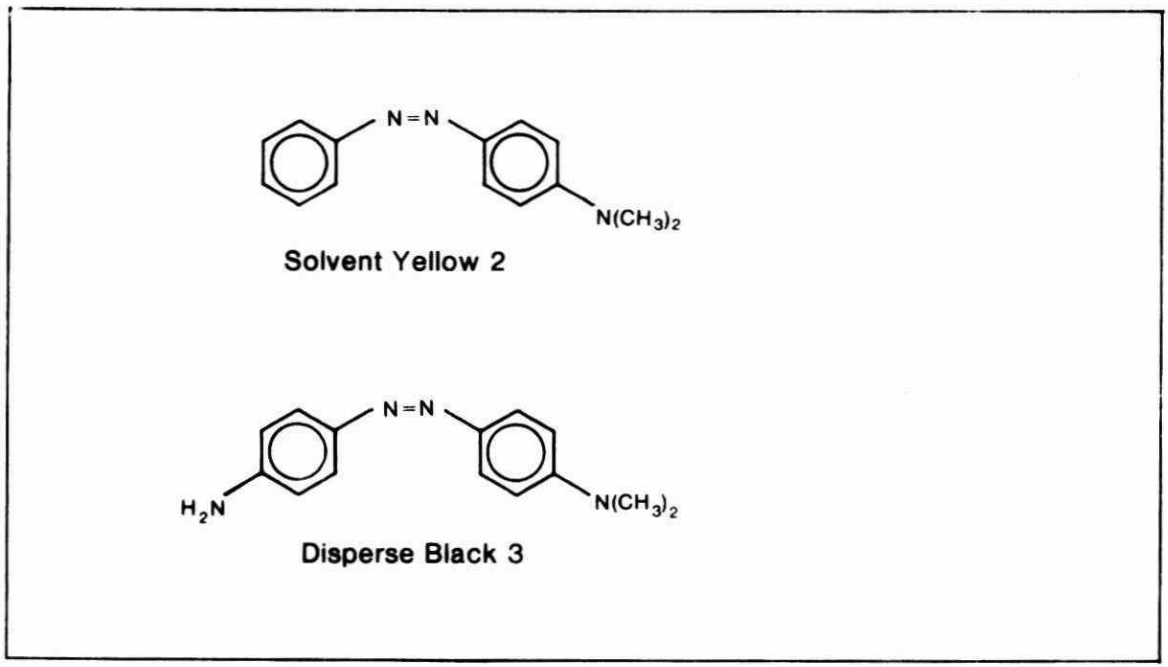


Figure 2.2.6 ILLUSTRATION SHOWING CHANGE OF COLOUR BY VARIATION OF CHROMOPHORE (AUXOCHROME)

Analogously, within the other ten major groups, similar auxochromic or chromophoric variations can be made to produce a virtual infinity of colours or shades.

TABLE 2.2.1

STRUCTURAL DESCRIPTIONS OF AZO DYES

Explanation of Symbols

A, a "diazo component", i.e. a diazotised arylamine

D, a "tetrazo component", i.e. a tetrazotised diamine

E, a coupling component coupled with one molecule of a diazo component

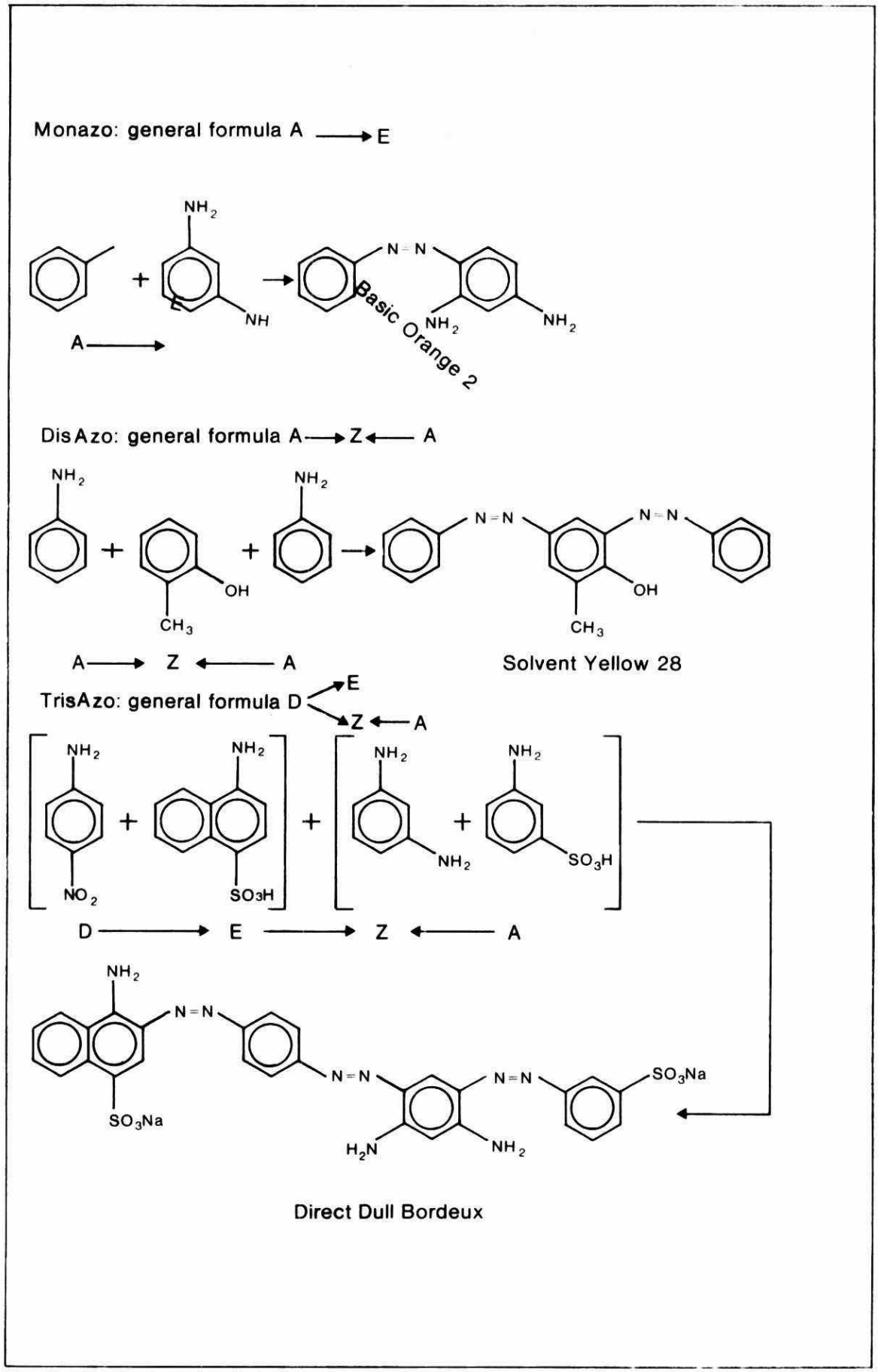
M, an aromatic amine which after coupling with a diazo component provides an amino group for further diazotisation

Z, a coupling component coupled with two (or more) molecules of a diazo component or with one molecule of each of two (or more) different diazo components

Z.X.Z, a binuclear coupling component capable of coupling with two molecules of a diazo component or with one molecule of each of two different diazo components

→ diazotised and coupled with

Class of Azo Compound		General Formula
Monoazo		A → E
Diazo	I	A → Z ← A'
	II	D → E, D → E'
	III	A → M → E
	IV	A → Z.X.Z ← A'
Trisazo	I	D → E, D → Z ← A
	II	D → E, D → M → E'
	III	A → Z, A' → M → Z
	IV	A → M → M' → E
	V	A → Z → A', A → Z → A"



Direct Dull Bordeux

Figure 2.2.4 SIMPLIFIED ILLUSTRATIONS OF SYNTHESIS OF SOME AZO DYE CLASSES

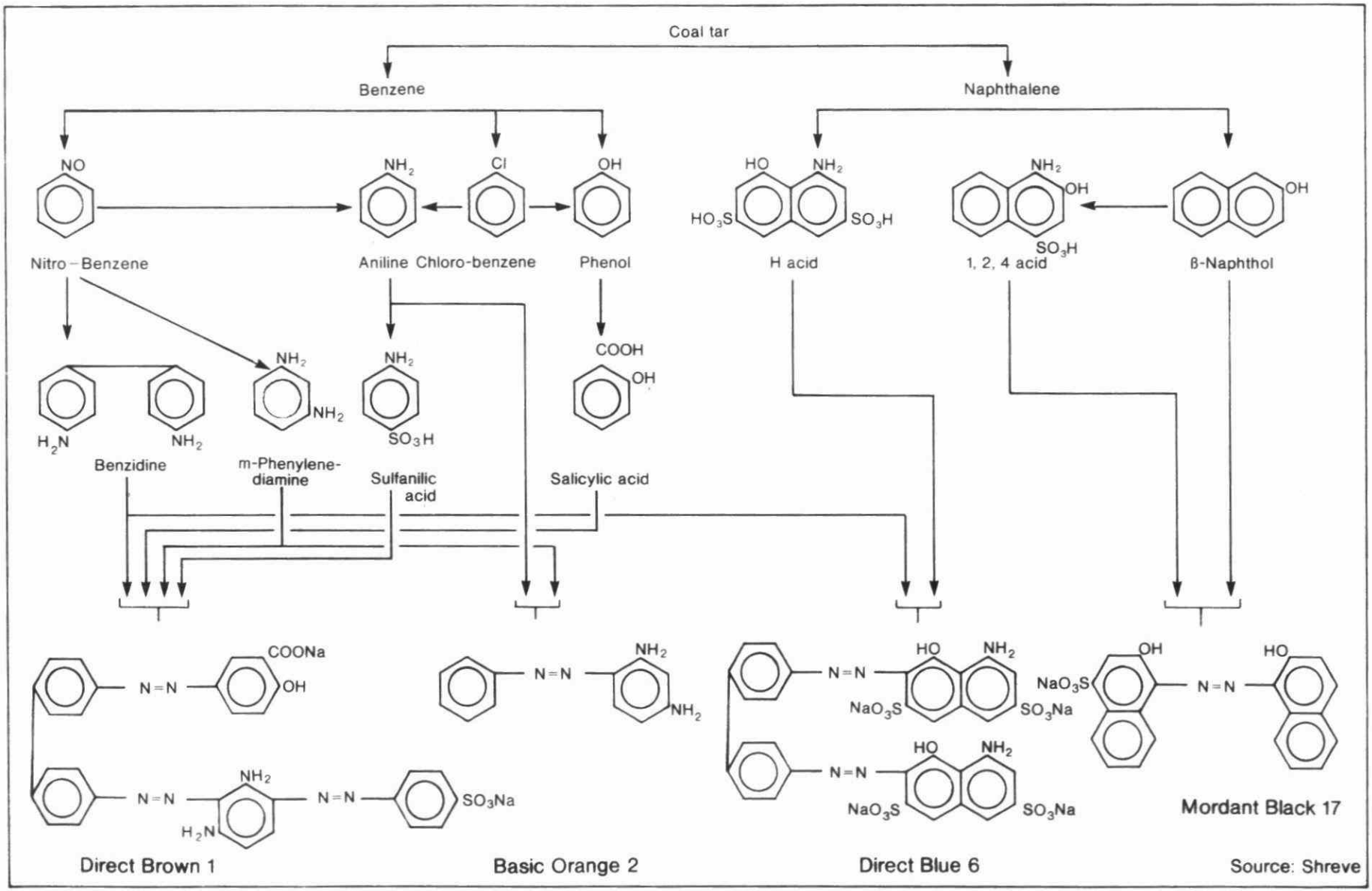


Figure 2.2.5
RELATIONSHIP BETWEEN SOME INTERMEDIATES AND AZO DYES

TOXICOLOGY 3

3.1 SYNOPSIS

From the standpoint of their toxicological effects, the most significant features of the aromatic amines and azo compounds are their ability to induce haemoglobin changes with resultant oxygen deprivation in the body organs and tissues, and their capacity to induce both malignant and non-malignant growths.

Other important toxic effects include local irritation of the skin and respiratory tract, induction of hypersensitivity affecting the skin and respiratory system, injury to the liver and kidneys, and anaemia.

Only five aromatic amines are presently recognized as carcinogenic in humans. These produce papillomas and cancer of the urinary bladder. These five amines are benzidine, 4-aminobiphenyl, auramine, beta-naphthylamine and N,N-bis(2-chloroethyl)-2-naphthylamine.

No cases of human cancer have as yet been attributed to any individual aromatic azo compound. However, a large number of aromatic amines and aromatic azo compounds have been found carcinogenic in experimental animals.

Cancers occur at the site of application with a few of these chemicals, suggesting that they act directly on the cells with which they come in contact. With most, however, the tumours appear in an organ quite remote from the site of application, indicating that metabolic products are responsible for the carcinogenic activity.

Present evidence suggests that all carcinogenic amines are first converted to N-hydroxy compounds (although all N-hydroxy compounds are not necessarily carcinogenic). The two major routes to the formation of N-hydroxy derivatives are: oxidation of a primary or secondary amino group; or reduction of a nitro, nitroso or N-oxide group. Both types of reactions are catalysed by enzymes. Some aromatic amines cannot be N-hydroxylated and are therefore non-carcinogenic. (5, chap. 8)

The N-hydroxy derivatives do not appear to be the ultimate carcinogenic chemical, since very few bind to proteins or nucleic acids. It appears that esterification of the N-hydroxy derivatives is the next step in converting the aromatic amines to their ultimate carcinogenic form, though further investigation is needed to confirm this. Esterification is also enzymatically mediated. Of the esters which may be formed, namely N-acetates, N-sulphates, N-carbamates, N-phosphates and N-glucuronides, a number have been shown to react in vitro with cellular macromolecules to form covalently bound derivatives. This binding is believed to occur by the dissociation of the ester to form an electrophilic molecule which then binds to the nucleophilic protein or nucleic acid molecules in the cell.

Oxidation at positions in the aromatic ring (C-hydroxylation) is also enzymatically mediated . The C-hydroxy derivatives as a group are less toxic than the primary or secondary amines. This reaction is the main metabolic route for detoxification of aromatic amines.

With regard to structure-activity relationships, no invariable correlations have been found. However, a number of generalizations can be drawn.

1. The monocyclic aromatic amines as a group are either non-carcinogenic or only weakly so. Potent carcinogenicity

is associated with aromatic compounds containing two or more conjugated or fused benzene rings.

2. Substitution in the ring position para to the amino group generally increases toxicity.

3. Substitution within the amino group can modify the carcinogenicity of the aromatic amine by interfering with N-hydroxylation. The effect on carcinogenic activation decreases in the order shown below. Letting X = an ester group, A = an alkyl group other than methyl, Ph = a benzene ring, (NO) = nitroso and (NO_2) = nitro, the relationships are:

$$OX > OH, (NO) > H, CH_3, NO_2 > COA > A > COPh > SO_2Ph.$$

4. Ring-substitution with methyl or methoxy groups ortho to the amine group often enhances carcinogenicity, whereas sulphonic acid derivatives are often non-carcinogenic.

5. In the case of aromatic azo compounds, cleavage of the azo bond is an important metabolic reaction, resulting in the formation of aromatic amine derivatives. The carcinogenic activity of azo compounds is due, in many instances, to their aromatic amine metabolites. However, in some cases the azo compound appears to be carcinogenic without undergoing prior cleavage.

3.2 BACKGROUND

3.2.1 Introduction

In this chapter of the report, the toxicology of the five primary group amines (aniline, benzidine, the naphthylamines, phenylenediamines and methylenedianiline) and of the azo dyes is presented under the headings:

(a) Absorption, Metabolism and Excretion
(b) Toxicity
(c) Carcinogenicity

This section on Health Effects is essentially a summary of the clinical findings noted primarily in men who have been occupationally exposed, supplemented by the results of experimental tests on animals.

Detailed consideration has been given to structure-activity relationships and bioactivation since there has been a considerable increase in research aimed at clarifying the metabolism of the aromatic amines and azo dyes. The objective of this research has been the determination of specific metabolites responsible for carcinogenic effects. An understanding of these sections pre-supposes some familiarity with the general concepts of toxicology and of certain biochemical and physiological reactions in the body. The background section has been included to summarize the essential points needed for comprehension of the later sections of this chapter.

3.2.2 Definitions

Toxicity

In a general sense, toxicity may be defined as the capacity of a substance to cause adverse health effects or injury to a living organism. Every chemical is toxic under certain conditions of exposure. A highly toxic substance will cause adverse health effects if administered even in small amounts. Substances of low toxicity will not produce adverse health effects unless the amount administered is very large. Thus, for any chemical, assessment of its toxicity must be related to:

(a) the quantity administered, i.e. the dose
(b) the route of administration, e.g. inhalation, ingestion, skin absorption, injection, etc.
(c) the distribution of the total dose in time, i.e. whether as a single or divided dose
(d) the nature and severity of the adverse effect
(e) the time needed to produce the adverse biological effect.

Hazard

Hazard may be defined as the probability or likelihood that a chemical will cause an adverse health effect under the conditions in which it is produced or used. Therefore, assessment of hazard has two principal components: exposure (or opportunity for intake) and toxicity.

Methaemoglobin

Methaemoglobin is formed when the ferrous iron of reduced haemoglobin is converted to the ferric form. The blue-black pigment which results is incapable of combining with oxygen, and therefore lacks the capacity of transporting oxygen to the tissues. In addition, the presence of methaemoglobin in the blood depresses the normal dissociation of oxyhaemoglobin, thereby further impairing the supply of oxygen to the tissues.

Methaemoglobinaemia is manifested clinically by the development of cyanosis. If severe, the oxygen deprivation of the brain and other organs can result in a form of asphyxiation.

Compounds which can produce methaemoglobinaemia by direct chemical reaction with haeme iron include nitrites, chlorates and quinones. Many aromatic amino- and nitro-compounds, while biologically inactive in themselves, can be

enzymatically converted to methaemoglobin-inducing agents(3). The relative methaemoglobin forming capacities of some 29 aryl amino- and nitro-compounds are tabulated by de Bruin (3).

3.2.3 Intake and Absorption

Environmental chemical compounds normally enter the body by inhalation, ingestion or absorption through the skin. Experimental investigation of toxicity may utilize these routes of entry, or employ various forms of injection of the chemical, e.g. subcutaneous, intramuscular, intravenous, intraperitoneal, or other means of administration such as intratracheal insufflation, bladder implantation, etc. In occupational exposure, inhalation is the most important route of entry, followed by skin absorption. Ingestion is of relatively greater importance in the case of exposure to chemicals which have entered food or water supplies.

With normal routes of entry, absorption into the blood stream is most rapid following inhalation, the slowest following skin application. However, this order is dependent on various physical and chemical properties of the specific substance.

Aside from chemicals which produce injury at the site of local application, e.g. acids and alkalis, the higher the concentration of the chemical in the body the greater its adverse effect. The concentration of the chemical in the body is, in turn, a function of:

(a) the total dose absorbed
(b) the rate of absorption
(c) the distribution of the chemical in the body
(d) the physical and chemical properties of metabolic products produced by its biochemical transformation
(e) the rate of biochemical transformation
(f) the rate of excretion of the chemical or its metabolites.

To reach the various organs and tissues of the body, the chemical must first be absorbed into the blood stream. This process requires that the chemical pass through several cell membrane barriers, e.g. through the cells of the alveoli in the lungs or of the epithelium lining of the gastro-intestinal tract, as well as the cells of the capillary walls, the blood cells and the various tissue cells. Absorption and excretion are thus dependent on the solubility of the chemicals in body fluids and on their ability to penetrate cell membranes.

The processes by which a chemical passes through a cell membrane are of three kinds: (a) diffusion, or passive transfer, in which the cell plays no active role; (b) active transport, in which the cell plays an active role in the transfer of dissolved chemicals; (c) phagocytosis and pinocytosis, in which undissolved particles are mechanically engulfed by the cell membrane.

Most chemicals can cross cell membranes by diffusion. The rate of transfer is determined largely by the lipid/water partition coefficient of the chemical, its concentration gradient across the membrane and its molecular weight. Chemicals in their ionized state are usually of low lipid solubility and have difficulty in penetrating the lipid cell membranes. However, in their un-ionized state, they may be lipid soluble and able to diffuse across cell membranes. The degree of ionization of the chemical is determined by its dissociation constant (pKa), which in turn is dependent on the pH of the medium in which the chemical is dissolved(1).

Active transport systems are characterized by the following features:

(a) the chemical can be transferred against a concentration gradient

(b) the chemical must have a certain molecular structure to be transported by the system
(c) metabolic inhibitors can block the transfer process
(d) inhibition of the transfer process can arise from the presence of competing chemicals transported by the same system.

3.2.4 Distribution

Chemicals administered by ingestion or by intraperitoneal injection are absorbed into the portal circulation and pass directly to the liver where they may undergo biochemical transformation.

Following passage through the liver, certain chemicals or their metabolites are excreted in the bile and re-enter the gastrointestinal tract to be excreted in the faeces or be re-absorbed. Other chemicals leaving the liver enter the general circulation and pass to other organs and tissues of the body.

Some chemicals are selectively concentrated or stored in specific organs or tissues, e.g. lead and radium in bone. Many become reversibly bound to plasma or tissue proteins by either of hydrogen, van der Waal's or ionic bonds. The liver and kidney have a high capacity to bind chemicals. For example, ligandin, a protein in the cytoplasm of the liver, has been found to bind azo dye carcinogens(1).

3.2.5 Metabolism

According to Parke and Williams (4) "the majority of chemicals normally regarded as foreign to the body are metabolized and transformed into other substances, irrespective of whether the foreign chemical is toxic or innocuous. In the case of toxic compounds, metabolism can play an important role in reducing or increasing the toxic effects, for a

compound may produce signs of poisoning either because it is toxic per se or because it is converted in the body into a toxic substance..... There are, however, compounds which do not undergo metabolic change in the body and obviously metabolism is not involved in their toxicity".

A few chemicals undergo biological transformation by direct chemical reaction with natural constituents in the body, e.g. the reaction of an alkylating agent with glutathione(2). However, for the majority of compounds which undergo metabolic change the process involves enzyme reactions. These appear to occur in two phases: Phase I reactions which comprise oxidations, reductions and hydrolyses; Phase II reactions which are classified as syntheses and comprise chemical conjugations.

In Phase I reactions the chemical acquires functional groups such as OH, NH_2, COOH and SH. These groups can facilitate Phase II synthetic reactions. If the chemical already contains any of these functional groups, it can undergo Phase II conjugations directly, without an initial Phase I reaction.

The major Phase II conjugation reactions(2) include:

- formation of glucuronides;
- formation of sulphate esters;
- O-, N-, and S-methylation;
- acetylations;
- formation of peptide conjugates;
- formation of glutathione conjugates and mercapturic acids;
- thiocyanate synthesis.

The metabolic transformation of a chemical may be relatively simple. It may consist of a single Phase I reaction which tends to increase the polarity of a compound and render it

more easily excretable. Other chemicals may undergo multiple reactions consisting of a combination of Phase I and a Phase II conjugations. These involve the addition of polar endogenous functional groups which render the compound more polar, less lipid soluble and more readily excretable.

Most of the metabolic changes of foreign chemicals occur in the liver, and to a lesser extent in those organs concerned with their absorption and excretion; i.e. the lungs, skin, gastro-intestinal tract and kidneys.

The enzymes which catalyse many of the Phase I and II biotransformations are present in (a) the microsomal fraction obtained from the endoplasmic reticulum (intracellular membranes) of cells of the liver, primarily, and of other organs; (b) in the mitochondria of liver and other cells; (c) in the soluble fraction of homogenized tissues; (d) in the plasma. For convenience, the enzymes are sub-divided into microsomal and non-microsomal classes.

Enzymes can be grouped by the chemical reactions which they catalyze, e.g. oxidations, reductions, hydrolyses and conjugations of various kinds. The ending "ase" is frequently used in naming enzymes to indicate their ability to catalyze a reaction. For example "oxidase" is an enzyme catalizing an oxidation.

Brief descriptions of biological transformation are given by Norton in Chapter 4 of Toxicology, by Casarett and Doull(1). The metabolic reactions affecting aniline, benzidine, the naphthylamines and the phenylenediamines, methylenedianiline and the azo dyes are described in Section 3.3.

Foreign compounds may also undergo metabolic change during passage through the gastro-intestinal tract through the action of intestinal microflora. Many of these reactions are Phase I reductions or hydrolyses.

Metabolic reactions which are mediated by enzymes are subject to factors which increase or decrease the activity of the enzymes. A change in enzyme activity could be the result of an alteration in the quantity of the enzyme and components taking part in the reaction, or to possible structural changes in the enzyme.

Chemicals which increase the activity of an enzyme system are known as inducers. If enzyme induction increases the formation of excretable or non-toxic metabolites the process will enhance detoxification. If it leads to the production of a more toxic metabolite, induction will increase the toxicity of the foreign chemical. With some chemicals maximum induction is achieved in 2 or 3 days; with other chemicals several weeks may be required to achieve maximum induction. Administration of a chemical in divided doses may result in induction, with a several-fold increase in the production of metabolites.

On the other hand, enzyme production may be depressed by certain chemicals, known as inhibitors. For instance, cytochrome P-450, an essential component of microsomal oxidation enzyme systems, is inhibited by carbon monoxide.

By altering the activity of one or more enzymes, or by competing for components in the enzyme system, inducers and inhibitors may alter the normal relationship between the various pathways by which a chemical is metabolized, with resultant alterations in the proportions of toxic and non-toxic metabolites produced.

Other factors which have been reported to influence the metabolism of foreign chemicals are:

- species differences; animal species may differ qualitatively and quantitatively in their enzyme systems, and thus metabolize a given chemical in different ways.

- strain differences; for example, four-fold differences in the rate of metabolizing aniline have been reported in different strains of rabbits(4).
- age; newborn and foetal animals metabolize some foreign compounds slowly because of low levels of many of the enzymes which metabolize Phase I and II reactions. Adult levels are reached in 4 weeks in the rat and in 8 weeks in humans.
- sex; in certain animal species toxicity to several chemicals has been found greater in one sex than in the other. Sex differences in the toxicity of warfarin and strychnine in the rat appear only after puberty, and are believed to be influenced by hormones.
- pre-existing liver disease.
- nutritional status.
- stress from exposure to heat or cold.

Chemical compounds which produce injurious effects promptly and at the site of application are in general considered to be toxic or carcinogenic per se. In the case of carcinogenicity, they are usually termed direct-acting, or primary or ultimate carcinogens.

Where injury is delayed for several hours, or occurs in organs or tissues remote from the site of application, the chemical has usually undergone metabolic transformation to produce a more toxic or carcinogenic compound. In this case the metabolite is considered the primary or ultimate carcinogen, and the original foreign chemical is referred to as a secondary carcinogen, a pre-carcinogen, procarcinogen or proximate carcinogen.

Other chemicals, which are not carcinogenic alone, but which increase the carcinogenic yield of known primary or secondary carcinogens are referred to as co-carcinogens or promoters.

3.2.6 Excretion

As mentioned previously, the metabolic transformation of foreign chemicals in the body usually results in the formation of compounds which are more polar, more water soluble, and less lipid soluble than the parent chemical. They are thus more readily excretable by the kidney.

Many chemicals are excreted in the bile, mostly as glucuronides or other conjugates. Excretion via the bile appears to be the major route when the molecular weight of the chemical or its metabolite exceeds 400. Compounds excreted into the bile pass into the gastro-intestinal tract where they may be excreted in the faeces. They may undergo further metabolic transformation by the intestinal flora to give derivatives which may or may not be toxic. These derivatives may be re-absorbed back into the portal circulation.

Some toxic chemicals, or their metabolites, may be excreted by other routes, such as expiration, sweat, milk, or exfoliation in hair, nail and epidermal cells.

3.3 HEALTH EFFECTS

3.3.1 Aniline

Absorption, Metabolism and Excretion

Aniline may enter the body by: inhalation of the vapour, ingestion, or by skin absorption of either the liquid or vapour. The rate of absorption of the vapour through the skin is comparable with that through the respiratory tract. Liquid aniline is absorbed through the skin at a rate of 0.2 to 0.7 mg per square centimetre per hour, with higher absorption at higher skin temperatures and if the skin is moist(11).

All animal species tested (ten, including man) oxidize aniline mainly to ortho- and para-aminophenol(7), the reaction occurring by microsomal oxidation in the liver. para-Aminophenol has been demonstrated to be the principal metabolite in man(11). Casarett and Doull(1) indicate this to be the major metabolic pathway, with the minor pathway being aniline to acetanilide to N-acetyl-p-aminophenol. Both derivatives are then conjugated. Phenylhydroxylamine (N-hydroxyaniline) and nitrosobenzene have been detected in the blood of cats and dogs after administration of aniline.

Aniline is excreted mainly through the kidneys in the form of the sulphuric and glucuronic acid conjugates of the ortho- and para-aminophenols. Other metabolites, such as acetanilide and the aminophenyl and acetylaminophenyl conjugates with mercapturic acid, have been found in the urine of some animals. It is possible that such metabolites are also present in the urine of people exposed to aniline. N-hydroxyaniline has not been found in the urine of animals after aniline administration. About 1% of absorbed aniline is excreted unchanged in the urine(11).

The urinary excretion of aniline metabolites has been found to give a fairly accurate measure of the absorption of aniline vapour through the skin and respiratory tract.

The metabolism and excretion of aniline takes place rapidly. According to Piotrowski(11), under conditions of repeated industrial exposure there should be no accumulation of aniline in the body.

Toxicity

Aniline, when applied locally, may act as a mild sensitizing agent and can cause dermatitis. Acute intoxication is due to methaemoglobin formation. The patient develops blue-grey

cyanosis if more than 20% to 30% of the haemoglobin in the blood is converted to methaemoglobin. Such levels can be achieved within 2 hours by skin absorption. Other symptoms are secondary to the methaemoglobinaemia, and include headache, weakness, malaise and anoxia. If absorption continues, coma and cardiac failure can result. Recovery has been reported after methaemoglobin concentrations of 70%(10). Occasional deaths have been reported from asphyxiation and at least one death from cirrhosis and atrophy of the liver has been reported. There is some question whether aniline is toxic to the liver and whether it can cause chronic poisoning by direct toxic action on the central nervous system.

Man is more sensitive than the rat to the methaemoglobin-inducing action of aniline. However, single oral doses of 5 and 15 mg of aniline had no effect on 20 adult humans(7). Inhalation of aniline vapour in concentrations of 100 to 160 ppm (380 to 608 mg/m^3) for 1 hour caused serious symptoms.

The LD_{50} for rats following oral administration is 440 mg/kg. The LD_{50} following skin absorption is 820 mg/kg for rabbits and 290 mg/kg for guinea pigs(19).

No reports of the LD_{50} for man by any route of absorption were found, but it probably does not differ significantly from that for the rat, according to Casarett and Doull(1).

The Threshold Limit Value (TLV) for aniline, as recommended by the American Conference of Governmental Industrial Hygienists (ACGIH), has been 5 ppm (19 mg/m^3) for many years. It is noted that at the 1978 annual meeting of the ACGIH it was proposed that the TLV be lowered to 2 ppm (10 mg/m^3). The USSR TLV is 1 ppm (5 mg/m^3).

Carcinogenicity

An increased incidence of bladder cancer in men employed in the aniline dye industry in Germany was reported in 1895, and has been confirmed by reports from Great Britain, France, Italy and the United States, as well as the USSR. Determination of the primary carcinogenic compound by epidemiological studies has been difficult. This is due to the exposure histories of the bladder cancer patients usually showing exposure to other aromatic amines in addition to aniline. A number of experimental studies, supplemented by detailed epidemiological investigations, have shown that exposure to 2-naphthylamine and benzidine were undoubtedly the most important contributors to the increased risk of bladder cancer in the aniline dye industry(7).

The International Agency for Research on Cancer (IARC) reviewed the animal evidence as to the carcinogenicity of aniline in 1973(7). It reported that aniline had not been found carcinogenic to rats following oral administration nor to mice by percutaneous injection. Recently, the U.S. National Cancer Institute has found that dietary administration of aniline hydrochloride at two dose levels induced haemangiomas and sarcomas and fibrosarcomas in several body organs of male and female Fisher rats, but not in the one strain of mice tested(59).

Some of the metabolites of aniline have been tested for carcinogenicity. para-Aminophenol and ortho-aminophenol-hydrochloride have been fed to rats and ortho-aminophenol has been implanted in the bladder of mice; no tumours were observed. Similarly N-hydroxyaniline and nitrosobenzene have failed to produce tumours in rats by percutaneous injection(7). After reviewing the epidemiological literature and experimental evidence, the IARC concluded in 1973 that there were no adequate data to indicate that aniline was carcinogenic in experimental animals and that it probably was not a carcinogen in man(7).

In the light of the recent report of the National Cancer Institute(59), the conclusions of the IARC respecting the carcinogenicity of aniline for experimental animals (rats) require reconsideration.

On the other hand, certain monocyclic aromatic monoamines, or their metabolites, have been found carcinogenic in aminals. Much of the evidence comes from the work of Weisburger et al(18). Ortho-toluidine which has an intraperitoneal (i.p.) LD_{50} of about 145 mg/kg in mice and 205 mg/kg in rats, produced subcutaneous sarcomas and bladder tumours in rats, and haemangiomas(18) and reticuloendothelial tumours in mice(5). meta-Toluidine, which has an i.p. LD_{50} of about 680 mg/kg in mice and 675 mg/kg in rats, and para-toluidine, which has an i.p. LD_{50} of about 418 mg/kg in mice and 325 mg/kg in rats, produced an increased incidence of liver tumours in mice(18). 4-Chloro-ortho-toluidine (i.p.. LD_{50} about 700 mg/kg in mice, 630 mg/kg in rats) while not carcinogenic in rats, produced haemangiosarcomas in mice(18)(9). 2,4,5-Trimethylaniline (i.p. LD_{50} about 410 mg/kg in mice) produced pulmonary and liver tumours in mice(18). 2,4,6-Trimethylaniline (i.p. LD_{50} about 315 mg/kg in mice, 540 mg/kg in rats) produced lung and liver tumours in rats and vascular tumours in mice; in addition, this compound also caused liver fibrosis in rats, though not in mice(18). 2,4-Xylidine (i.p. LD_{50} about 455 mg/kg in mice, 575 mg/kg in rats) produced an increase of pulmonary tumours in female mice, though not in male mice or in male rats. 2,5-Xylidine (i.p. LD_{50} about 836 mg/kg in mice, 810 mg/kg in rats) produced suggestive increases of subcutaneous tumours in male rats and vascular tumour in male mice(18).

3.3.2 Phenylenediamines

Absorption, Metabolism and Excretion

Both para- and meta-phenylenediamine are absorbed through the skin. No reference to the dermal absorption of the ortho isomer was found. All three isomers may enter the body by inhalation or ingestion. meta-phenylenediamine is not metabolized in man and is excreted rapidly in the urine. In dogs, para-phenylenediamine is excreted in part as N,N'-diacetyl-para-phenylenediamine(9).

It is of some interest that para-phenylenediamine is excreted as a metabolite in urine of dogs and rats following oral and subcutaneous administration of para-dimethyl-aminoazobenzene.

Toxicity

para-Phenylenediamine is a skin irritant and a well-known allergen. It is a fairly common cause of allergic dermatitis, and may cause asthma and other respiratory symptoms as well as kerato-conjunctivitis affecting the eyes. Systemic poisoning is uncommon, but gastro-intestinal and nervous system symptoms have been reported. One female hairdresser is known to have died of subacute liver atrophy following 5 years of using para-phenylenediamine hair dyes. Subcutaneous injection of para-phenylenediamine hydrochloride has produced muscle lesions in rats(9).

Both the meta and ortho isomers are considered less toxic then para-phenylenediamine.

The oral LD_{50} of para-phenylenediamine is 100 mg/kg in cats and 250 mg/kg in rabbits. Its ip. LD_{50} in rats is 37 mg/kg(9). The oral LD_{50} in rats, as an oil in water emulsion is 80 mg/kg.

The oral LD_{50} of meta-phenylenediamine in rats, as an oil in water emulsion, is 650 mg/kg(9). Its i.p. LD_{50} in rats is reported to be 283 mg/kg(9) and 325 mg/kg(18).

The i.p. LD_{50} of ortho-phenylenediamine is 290 mg/kg(18).

The TLV for para-phenylenediamine recommended by the ACGIH is 0.1 mg/m^3. TLV's for the meta or ortho isomers have not been identified.

Carcinogenicity

There have been no reports of malignancy in humans associated with the manufacture or use of para-or meta-phenylenediamine. Animal experiments have been inadequate for full evaluation of the carcinogenicity of these amines, though two reports (by the same investigators) mention fibrosarcomas occurring at the site of injection following subcutaneous administration of both the para and the meta isomers(9). Weisburger et al(18) found meta-phenylenediamine inactive when fed to male rats and male and female mice. ortho-Phenylenediamine produced an increase of liver tumours in rats and mice following ingestion.

3.3.3 2,4-Diaminotoluene

Absorption, Metabolism and Excretion

2,4-Diaminotoluene is absorbed after ingestion. Information was not readily available as to its absorption through the skin or by inhalation. Its risk by the latter route would appear to be low in view of its low vapour pressure (1 mm at 106.5°C).

In rodents the major urinary metabolite is 2,4-diamino-5-hydroxytoluene. N-acetyl and glucuronide conjugates are also found in the urine(9). Acetylation of the amine is mediated by an N-acetyl transferase present in the liver, kidneys, lungs and intestional mucosa.

Excretion in rats is rapid during the first 7 hours after intraperitoneal administration. Over 75% of the i.p. dose is excreted via the kidneys, and about 22% in the faeces(9).

Toxicity

2,4-Diaminotoluene is a methaemoglobin inducer. The i.p. LD_{50} is about 85 mg/kg(18). No recommendation has been made by the ACGIH as to a TLV.

Carcinogenicity

2,4-Diaminotoluene is carcinogenic in rats, producing liver cancers after oral administration and local sarcomas after subcutaneous injection(9). Weisburger et al(18) found an increase in subcutaneous fibromas in rats following oral administration, as well as an increase in liver tumours. In mice there was an increased incidence of liver cancers. There are no reports of the carcinogenicity of 2,4-diaminotoluene to man.

From the foregoing review of the carcinogenic effects of monocyclic aromatic amines it is apparent that, as stated by Clayson and Garner(5), the experimental evidence leaves "no doubt that single-ring aromatic amines under appropriate dosages may be carcinogenic". The dosages used in these experiments were very high in comparison to the levels of intake likely to occur in humans exposed through environmental contamination.

None of the monocyclic aromatic amines discussed above have been found, as yet, to be carcinogenic in man. However, there have been reports from Sweden, Australia and the United States, as noted by Clayson and Garner(5), that excessive intake of analgesic compounds containing the monocyclic amine phenacetin, as well as other amines, was associated with cases of urinary tract cancer. Experiments to deter-

mine whether phenacetin is carcinogenic in animals and, if so, at what dosages and by what metabolic pathways would be of some significance in assessing the risk to humans of exposure to other monocyclic aromatic amines.

3.3.4 4-Aminobiphenyl

4-Aminobiphenyl is apparently no longer commercially produced. However, because of its structural similarity to benzidine, it is relevant to note that an increased incidence of bladder cancer has been reported in one group of men occupationally exposed to this compound. This amine has also been found to be carcinogenic in the mouse, rabbit and dog following oral administration, and the rat following subcutaneous injection(6).

In rats, 4-aminobiphenyl is N-hydroxylated to N-hydroxy-4-acetamidobiphenyl(6). The same metabolite was found in the urine of rabbits and cats treated with 4-aminobiphenyl(28). In dogs, it is converted to 4-amino-3-biphenyl hydrogen sulphate and 4-amino-3-biphenyl-B-D-glucuronic acid(6), as well as to the C-ring hydroxylamine and to nitroso derivatives(5).

The metabolite N-hydroxy-4-acetamidobiphenyl has been found carcinogenic in animals by conventional testing techniques, and other metabolites have demonstrated carcinogenic effects by bladder implantation in mice or when injected into newborn mice(5,6). Clayson and Garner(5) have tabulated the carcinogenic effects of a large number of congeners of 4-aminobiphenyl. It is of some interest that 4-nitrobiphenyl, which is readily reduced to 4-aminobiphenyl, has also induced bladder cancer when given orally to dogs, the only species and route of administration tested(7). There are no data as to the carcinogenicity of 4-nitrobiphenyl in man.

3.3.5 Benzidine

Absorption, Metabolism and Excretion

Benzidine, or 4,4'-diaminobiphenyl, can be absorbed from the lungs following inhalation of solid or liquid aerosols, and from the gastro-intestinal tract following ingestion. Meigs et al(12) considered skin absorption the route of major importance in industrial exposure.

In the body, benzidine is metabolized mainly to 3-hydroxy-benzidine and to its N-acetyl derivative. Other metabolites formed are mono- and diacetylbenzidine. Haley(15) lists the various metabolites of benzidine found in a number of animal species. Acetylation of benzidine has not been observed in dogs(6).

In humans, benzidine is excreted in the urine, partly unchanged (3.6 to 5.6% of total excretion products), partly as mono- or diacetyl benzidine (6.7 to 15.9%), and the rest as the N-sulphuric and N-glucuronic conjugates of 3-hydroxybenzidine(13).

Systemic accumulation of benzidine in man after repeated exposure appears unlikely. The half-time for the elimination of benzidine has been estimated to be 20 hours in rabbits, 5.8 hours in dogs, and 5.4 hours in man (quoted in 11).

Toxicity

Benzidine is said to cause haemolysis of the blood and depression of bone marrow activity. On ingestion, it can cause nausea and vomiting, followed by liver and kidney injury. Other symptoms include inflammation of the bladder and haematuria. Benzidine is not included in de Bruin's list of methaemoglobin-inducing aryl amino-compounds, nor are any

other biphenyl compounds listed(3). Methaemoglobin formation is not mentioned in Haley's review of the problems associated with the use of benzidine and its congeners(15).

The oral LD_{50} in the rat is 309 mg/kg, and in the mouse is 214 mg/kg.

Benzidine has been classed by the ACGIH as a human carcinogen, without an assigned TLV.

Carcinogenicity

An increased incidence of bladder cancers in workmen exposed to benzidine in Great Britain was reported in 1954. Cases of bladder cancer attributable to benzidine have also been reported from Italy and the United States. Experimentally, benzidine has been found carcinogenic to the bladder in dogs and to the liver in rats and hamsters following oral administration. Subcutaneous injection has produced liver cancer in rats and mice, and colon cancers, acoustic duct cancers and sarcomas in rats(6).

Cancers of the liver, colon, stomach, acoustic duct and bladder have been produced by 3,3'-dihydroxybenzidine (quoted in 16). These results were questioned by Clayson (17), whose group failed to show that 3,3'-dihydroxybenzidine was carcinogenic in mice. Clayson and Garner(5) list the benzidine derivatives which have been found carcinogenic to various organs when administered to several different species of animals. Their list includes:

- 3,3'-dichlorobenzidine (reviewed in detail in Ref. 7, p.87);
- 3,3'-dimethoxybenzidine (ortho-dianisidine, reviewed in Ref. 7, p.41);
- 3,3'-dimethylbenzidine (reviewed in Ref. 6, p.87);
- N,N'-diacetylbenzidine (reviewed in Ref. 9, p.293);
- 2-methyldiacetylbenzidine;
- 3,3'-benzidinedicarboxylic acid.

Haley's review also lists 3,3'-benzidinedioxyacetic acid(15).

3.3.6 Methylenedianiline (MDA)

Absorption, Metabolism and Excretion

Little information was found on the absorption of MDA or on its metabolism. Dunn and Guirguis(20) considered skin absorption the main route of entry in 11 cases of jaundice occuring in Ontario workers between 1967 and 1976. MDA can enter the body by inhalation and ingestion. When dissolved in propylene glycol and injected intra-peritoneally in animals (species not identified), about 25% appears in the bile in the form of 3 or 4 unidentified metabolites(7).

Toxicity

MDA is slightly irritating to the respiratory system at concentrations of 0.5 to 1 ppm. It is painfully irritating to the eyes at 4 ppm(58).

MDA is toxic to the liver and to the kidneys. Single oral doses of 10 mg/kg have been reported to cause liver and kidney damage in rats, and chronic oral administration of 3 mg/kg to cause cirrhosis of the liver and blood abnormalities. There are at least four reports in the literature of hepatitis and jaundice in workmen who were occupationally exposed to MDA(20,58).

The oral LD_{50} for rats given MDA in solution is 830 mg/kg(58). Dunn and Guirguis(20) have suggested a TLV of 0.04 mg/m^3. The ACGIH recommended a TLV of 0.1 ppm (0.8 mg/m^3 and a Short-Term Exposure Limit of 0.5 ppm (4 mg/m^3) in 1978(58). These recommendations are awaiting formal adoption.

Carcinogenicity

There are no reports of cancer associated with human exposure to MDA, and only equivocal evidence (3 reports) as to its carcinogenicity in rats following oral and percutaneous administration(7).

A congener, 4,4'-methylene-bis-(2-chloroaniline) has been found carcinogenic in the mouse and rat after oral administration and produced distant tumours in the rat after subcutaneous injection(7).

Two studies on men who were occupationally exposed failed to show evidence of an increased risk of bladder cancer; this may have been due to too short a period of follow-up(7). This amine is on the Occupational Safety and Health Administration's (OSHA) draft list of confirmed carcinogens(22).

A second congener, 4,4'-methylene-bis-(2-methylaniline) has also been reported as carcinogenic to rats following oral administration, the only species and route tested. There are no reports of its carcinogenicity in man(7).

Auramine, which is structurally similar to MDA, has produced liver tumours in mice and rats following oral administration, and an increased incidence of bladder cancer has been reported in men engaged in its manufacture(6).

An increased incidence of bladder cancer has also been reported in men employed in the manufacture of magenta (fuchsine), a mixture of three closely-related 4,4',4"-triamino-triarylmethane dyes, though not in men engaged in its purification or use. The affected men were believed not to have had concomitant exposure to benzidine or naphthylamine, but they may have had concomitant exposure to ortho-toluidine. In one experiment, para-magenta (no CH_3 groups) produced local sarcomas in rats in which it was injected subcutaneously(7).

3.3.7 Naphthylamines

Absorption, Metabolism and Excretion

The naphthylamines may enter the body by inhalation, ingestion and by absorption through the skin. Within the body, beta-naphthylamine undergoes metabolism via four pathways(6):

1. N-hydroxylation followed by conversion to 2-amino-1-naphthylmercapturic acid, 2-nitrosonaphthalene and rearrangement to 2-amino-1-naphthol.
2. Oxidation at C_5 and C_6 to an arene oxide which rearranges to 5-hydroxy-2-naphthylamine, reacts with water to form a 5,6-dihydroxy-dihydro derivative which forms a 5-hydroxy-6-mercapturic acid.
3. Conjugation of the amino group with acetic, sulphuric or glucosiduronic (sic, presumably glucuronic) acid.
4. Secondary conjugation of the hydroxyl group with phosphoric, sulphuric or glucosiduronic (sic) acids.

Nearly thirty metabolites have been identified in the urine of rats, rabbits, dogs and monkeys following beta-naphthylamine administration(5). In most species 2-amino-1-naphthylsulphate is the predominant metabolite. In man, N-(2-naphthyl)-hydroxylamine and bis-(2-amino-1-naphthyl)phosphate have been identified as excretion products in urine.

The metabolism of alpha-naphthylamine has not been extensively studied. Conjugates of 1-amino-2-naphthol and 1-amino-4-naphthol have been reported in several species. N-hydroxylation and the formation of methaemoglobin appear to occur much less readily following low doses (5 mg/kg) of alpha-naphthylamine given orally to dogs than occurs with similar doses of beta-naphthylamine. At high levels (70 mg/kg) about the same proportion (0.2%) of each isomer is

converted to the corresponding N-hydoxylamine and nitroso compounds(6). In man, oral administration of alpha-naphthylamine has resulted in the excretion of N-hydroxy-N-(1-naphthyl) acetamide either in the free state or conjugated with glucuronic acid(7).

Toxicity

Both alpha- and beta-naphthylamine cause methaemoglobinaemia in proportion to the amount of N-hydroxy compounds formed.

The oral LD_{50} in rats for alpha-naphthylamine is 779 mg/kg and for beta-naphthylamine is 727 mg/kg. No TLV is given for alpha-naphthylamine by the ACGIH. Beta-Naphthylamine is classed as a human carcinogen without an assigned TLV.

Carcinogenicity

From epidemiological studies reported in England and in the United States, there is strong evidence of a greatly increased risk of bladder cancer in men exposed to beta-naphthylamine both pure or as an impurity with other compounds. Given orally, this isomer has produced bladder cancer in dogs, monkeys, and with large doses, in hamsters. Given orally to mice it has produced liver cancers; when administered to mice by subcutaneous or intramuscular injection it has induced liver cancers and local sarcomas. The latter occurred after the beta-naphthylamine had been allowed to age in arachis oil, suggesting that oxidation products may have been responsible for the local carcinogenic effects(7). Oral administration of beta-naphthylamine did not induce cancers in the rat, rabbit or cat(5).

Occupational exposure to alpha-naphthylamine containing 4% to 10% of beta-naphthylamine has been found to be associated with an increased risk of bladder cancer in man. Whether pure alpha-naphthylamine is carcinogenic in humans is at present not known.

The results of carcinogenicity testing in animals given alpha-naphthylamine are inconclusive(7). However, the Occupational Safety and Health Administration (OSHA) in the

United States has included alpha-naphthylamine, as well as beta-naphthylamine, in its draft list of Class I confirmed carcinogens (269 chemicals for which two or more reports of carcinogenic or neoplastic effects were found in the literature)(22).

There has been extensive experimental research on the metabolism and carcinogenicity of naphthylamine derivatives since the mid-1950's. The carcinogenic effects have been tabulated by Clayson and Garner(5). Local tumours have been produced by 2-naphthylhydroxylamine following dermal application in mice and intraperitoneal injection in rats. 1-Naphthylhydroxylamine also induced local tumours in mice following skin application, and in rats after ingestion. Other beta-naphthylamine derivatives showing carcinogenic activity in mice or rats include the 1-methoxy-, 2-methyl- and 3-nitro- substituents and N,N'-bis(2-chloroethyl)-2-naphthylamine. Tumours were not induced by 1-fluoro-2-naphthylamine, nor by the alpha-naphthylamine derivatives, 1-naphthylacetamide and 1-naphthylacethydroxamic acid(5). A recent review of the carcinogenicity of N-phenyl-2-naphthylamine(9) suggests that this compound is carcinogenic to mice, and may have contributed to an increased risk of bladder cancer in rubber workers not occupationally exposed to beta-naphthylamine. N-Phenyl-2-napthylamine is metabolized to beta-naphthylamine in man and dogs(60).

3.3.8 N,N'-bis-(2-chloroethyl)-2-naphthylamine

This amine has proven carcinogenic to the mouse lung following intraperitoneal injection, and has a local carcinogenic effect in rats following subcutaneous injection(7).

In humans to whom this drug has been administered with ^{32}P sodium phosphate for the treatment of polycythaemia and neoplasms of the haemopoietic system, follow-up studies have shown a high incidence of bladder tumours(7).

3.3.9 Other Aromatic Amines

Data relating to the carcinogenicity of some 32 other aromatic amines have been reviewed by the International Agency for Research on Cancer(9). Of these, eight are used primarily as hair dyes, nine as colouring agents. Fifteen are classed as miscellaneous industrial chemicals. (See Appendix IV).

3.3.10 Aromatic Azo Compounds

The azo compounds, which contain the -N=N- group, are coloured and have been used for many years as dyestuffs for fabrics, in the printing trade, and as colourants for foods and drink. Some have been used as therapeutic agents in medicine, or as intermediates in the manufacture of drugs.

The textile dyes in which aromatic azo compounds may be present include direct dyes, disperse dyes, azoic dyes, acid dyes and basic dyes(24). The hair colourants which may contain azo compounds include direct dyes and disperse dyes. The majority of food colourants are acid or basic dyes which ionize readily and are not easily absorbed into the blood stream from the gastro-intestinal tract.

Absorption, Metabolism and Excretion

There appears to have been little research on the absorption of aromatic azo compounds through the skin or via inhalation. The most common route of entry is by ingestion of food colourants. Inhalation and skin absorption are of greater importance in persons who are occupationally exposed.

The metabolism of the simpler aromatic azo compounds, such as the aminozbenzene dyes, has been extensively studied. This is due to the discovery that many are carcinogenic in experimental animals.

Five kinds of reactions are involved in the metabolism of N,N-dimethylaminoazobenzene (DAB)(3). These are:

(a) Reductive scission at the azo linkage
(b) N-demethylation
(c) N-hydroxylation
(d) Ring (C)-hydroxylation
(e) N-acetylation combined with conjugation of metabolites

Except for the N-hydroxylation reaction, these metabolic changes are considered to be deactivation routes through the formation of excretable metabolites. These are mainly the glucuronide, sulphate or acetate conjugates.

Reductive cleavage of the azo bond yields aromatic amines. This process is catalyzed by an azoreductase microsomal enzyme in the liver, and also, to an important degree, by the flora in the gastro-intestinal tract. With DAB, up to 60% of the administered dose in rats is excreted as the acetate conjugates of p-aminophenol and p-phenylenediamine. Minor urinary metabolites include methylation products of p-phenylenediamine. N-demethylation of DAB is evident from the presence of appreciable amounts of N-monoaminoazobenzene (MAB) and 4-aminoazobenzene (AB) in the liver, and of these metabolites and their 4-hydroxy derivatives in the urine and bile of DAB-treated rats. C-hydroxylation of DAB occurs at several positions of the aromatic ring, resulting ultimately in the formation of 2-, 3-, and 4-hydroxy derivatives (mostly sulphates) of DAB, MAB and AB. These are found in the urine, liver and bile of treated rats. N-demethylation and C-hydroxylation appear to occur prior to the reductive scission of the azo bond, according to de Bruin(3). In the

case of DAB, Clayson and Garner(5), give the sequence of reactions in somewhat different order, namely; stepwise N-demethylation, followed by N-acetylation, C-hydroxylation, and reduction scission to give p-aminophenol and p-amino-acetamide.

In the N-hydroxylation of the N-dialkylaminoazobenzene compounds, N-demethylation appears to be a prerequisite. The sequence of reactions appears to be: transformation of the N-alkyl group to the N-hydroxyalkyl group, then demethylation by release of formaldehyde followed by the formation of the N-hydroxy metabolite. There is some debate as to which intermediate or product represents the activated carcinogenic metabolite of DAB.

While the metabolism of other aromatic azo compounds has been subject to comparatively little research, the reactions outlined for DAB have been demonstrated for some other methylaminoazobenzene compounds, such as 3'-methyl-DAB, and are believed to apply to other aromatic azo compounds.

Two nitroazobenzene dyes, Para Red and Dinitroaniline Orange, have recently been shown to be mutagenic(23) whereas the metabolites which would have been expected after splitting the azo bond (p-nitroaniline, 1-amino-2-naphthol and 2,4-dinitroaniline) are not mutagenically active. It thus appears that for the nitroazobenzene compounds reductive scission may not be a necessary step in their carcinogenic activation.

There is little information available regarding the excretion of most specific aromatic azo compounds. However, it is known that those which are readily ionizable, such as the sulphonic acid salt type dyes and the basic dyes, are absorbed from the gastro-intestinal tract only with difficulty. On ingestion, the greater part of such compounds is excreted unchanged in the faeces. Azo compounds which are

cleaved by the action of the intestinal flora or by the nitroreductase system in the liver, to form aniline and benzidine derivatives, will be excreted in the urine and faeces as outlined in the section of the report dealing with aromatic amines.

Toxicity

Because of the very large number of existing aromatic azo compounds and the lack of readily available toxicological information on many of them, it is possible to discuss their toxicity only in general terms. Most of our understanding of their toxicological effects comes from their use as therapeutic agents, often when taken in overdose, and from research on the carcinogenicity of the N-methylaminoazobenzenes.

Some of the aromatic azo compounds act topically on the skin, producing contact dermatitis, e.g. p-aminoazobenzene (DAB)(8). Inhalation of some compounds can produce pulmonary irritation. Allergic responses, such as urticaria and asthma, have been reported. When absorbed into the body some compounds, such as aminoazobenzene, the N-methylaminoazobenzenes and pyridium, produce methaemoglobinaemia. It is probable that, with larger doses, many are toxic to the liver. This has been demonstrated with DAB and pydridium, for example. Other effects which have been reported include kidney failure and haemolytic anaemia(8).

Carcinogenicity

No human cases of cancer have as yet been attributed to any individual aromatic azo compound(1). Experimentally, a large number of aromatic azo compounds have proven to be carcinogenic. These compounds usually produce tumours, not at the site of application, but in a remote organ or system

such as the liver (usual in rats) or the liver and urinary bladder (usual in mice, hamsters and dogs). In general, if the aromatic azo compounds contain polar substituents such as the sulphonic acid group they are usually, though not always, non-carcinogenic.

Much of the variation in the carcinogenic activity of the aromatic azo compounds is explained by the susceptibility of the particular molecule to scission at the azo bond, and to the metabolic detoxification or activation of the scission products, many of which reactions are enzyme-mediated.

The simplest aromatic azo compound, azobenzene (which has an oral LD_{50} for rats of 1000 mg/kg) has usually been considered non-carcinogenic(17) but the International Agency for Research on Cancer notes that ingestion of this chemical produced liver cancers in male mice of one strain, though not in female mice or in rats(8).

The carcinogenic effects of a large number of other aromatic azo compounds are discussed by Clayson and Garner(5), who classified then into three groups, viz.:

(a) Amino compounds with an unsubsituted amino group, i.e. derivatives of 4-(phenylazo)aniline;
(b) Aminoazo compounds in which the amino group is methylated, i.e. derivatives of N,N-dimethyl-4-(phenylazo)-aniline;
(c) A miscellaneous group of azo dyes used in food and medicine.

Of twenty-one 4-(phenylazo)aniline compounds, 5 were carcinogenic: 4-(phenylazo)aniline, 4-(phenylazo)-o-anisidine, 4-(o-tolylazo)-o-toluidine, 2-(o-tolylazo)-p-toluidine and 4-(p-tolylazo)-m-toluidine. It is of interest to note that 4-(phenylazo)-N-phenylhydroxylamine was not carcinogenic whereas the structurally similar 4-biphenylhydroxylamine was

carcinogenic, producing liver tumours when injected subcutaneously into newborn mice. Similarily, 4-(phenylazo)-N-phenylacethydroxamic acid was not carcinogenic to the rat where as 4-biphenylacethydroxamic acid was carcinogenic.

Among sixty-six N,N-dimethyl-p-phenylazoaniline compounds tested in rats, 42 were carcinogenic, 24 were not.

Of the miscelleneous group of azo dyes, Clayson and Garner listed 7 which were carcinogenic. These were: 1-phenylazo-2-naphthol, 1-o-tolylazo-2-naphthol, Citrus Red No. 2, Ponceau 3R, Ponceau MX, Trypan Blue and Evans Blue.

The evidence as to the carcinogenicity of 32 aromatic azo compounds was reviewed by the International Agency for Research on Cancer(8). (See Appendix IV).

3.4 STRUCTURE-ACTIVITY RELATIONSHIPS

3.4.1 Introduction

The structural characteristics of the carcinogenic aromatic amines, grouped according to the structures of five basic molecules, are presented in Tables 3.4.2 to 3.4.6. These molecules are illustrated in Figure 3.4.1 and it is suggested that the reader refer to these illustrations as he interprets the tables. The method of presentation follows that of de Bruin(3) but, in view of the results of recent studies and the consequent need for greater flexibility, we have modified his method of indicating the molecular position of substituent groups by designating the carbon atoms of the aromatic rings in the conventional numerical manner. Substituents on the NH_2 group appearing in the tables are designated "R", or "R_1" and "R_2".

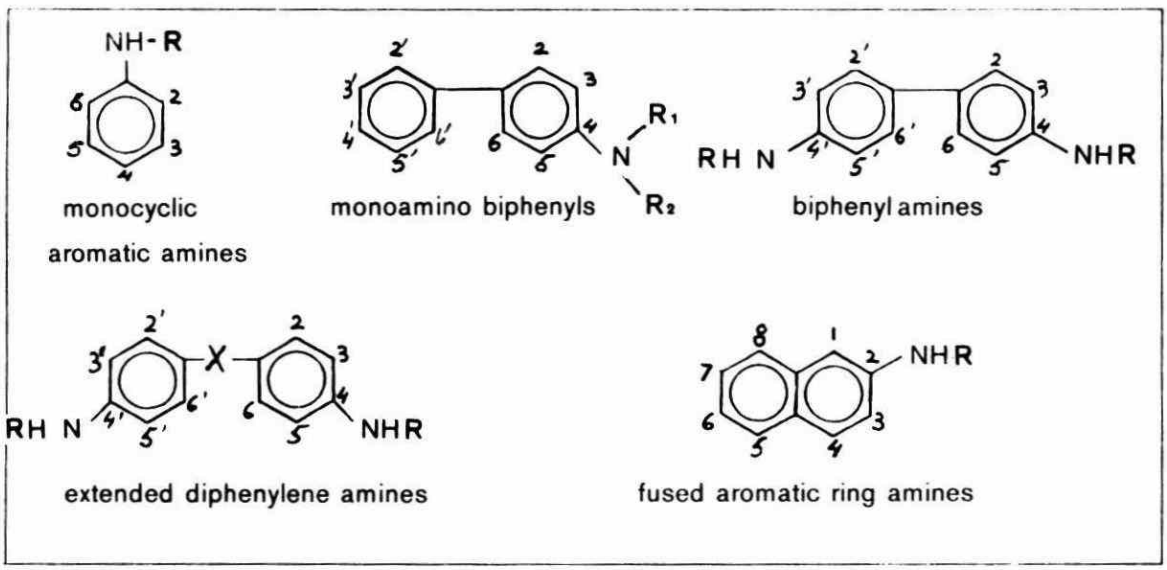


Figure 3.4.1. Illustration of classes of amines referred to in Tables 3.4.2 - 3.4.6.

TABLE 3.4.1

LEGEND FOR TABLES 3.4.2 - 3.4.6

ROUTE

o	=	oral
i.p.	=	intraperitoneal
s.c.	=	subcutaneous
sk	=	skin
bl	=	bladder instillation

SPECIES

1	=	mouse
2	=	rat
3	=	rabbit
4	=	hamster
5	=	dog
6	=	monkey

ORGAN

A	=	Acoustic Duct
Bl	=	Bladder
Bo	=	Bone
Br	=	Breast
I	=	Intestine
K	=	Kidney
Li	=	Liver
Lo	=	Local
Lu	=	Lung
Ly	=	Lymphoma
MO	=	Multiple Organs
Pa	=	Pancreas
Pi	=	Pituitary
Sc	=	Subcutaneous
SG	=	Salivary Gland
Sk	=	Skin
St	=	Stomach
Va	=	Vascular

In addition to showing the compounds formed by the introduction of various substituent groups, the tables also indicate the routes of administration and the animal species used, and the organs in which malignancy was induced. Table 3.4.1 provides a key to the symbols used in the five subsequent tables. For some derivatives a query has been placed before the name of the organ affected to indicate doubt as to the validity of the carcinogenic effect in view of variations in response in repeat experiments or of the findings in control animals. Those compounds marked with an asterisk are considered carcinogenic to humans.

Inclusion in the tables of data on the doses of test substances shown to be carcinogenic was found to be impractical because of the need to relate the dose to (a) acute or chronic intake, (b) route of administration, (c) species and strain of animal used, (d) the age and sex of the test animals, (e) adequacy of diet, (f) the normal incidence of malignancy in various organs in the control animals, and (g) the validity of tests of the statistical significance of any increase in the test animals over the normal incidence in the controls. In addition, it is considered that the dose-response data from such animal experiments would be of very limited value when attempting to infer the degree of risk to man.

In tabulating the results of carcinogenicity testing, investigations in which positive effects were obtained only after bladder implants in which the chemical was incorporated in paraffin or cholesterol pellets have been discounted. Clayson and Garner(5) have pointed out that the validity of this method of testing has been questioned because the vehicle itself produced changes in the bladder epithelium and variable tumour induction.

The compounds tabulated do not represent a comprehensive list of all the derivatives reported to produce carcinogenic effects, but rather indicate the major groups of active compounds. The primary sources of information used in compiling the tabulations were Clayson and Garner(5), the IARC monographs(6,7,8,9) and Weisburger et al(18).

3.4.2 Monocyclic Aromatic Amines

As indicated earlier, several aniline derivatives exhibit weak-to-moderate carcinogenic activity at relatively high dose levels in one or more species of experimental animals. At present there is no definite evidence for their carcinogenicity in humans.

Presented in Table 3.4.2 is a listing of carcinogenic monocyclic aromatic amines.

The following generalizations regarding the carcinogenicity of the monocyclic aromatic amines may be drawn from an examination of the effects of introducing various functional groups into the aniline ring:

1. Introduction of a methyl group at the ortho or para positions increases carcinogenicity. Introduction of a methyl group at the meta position results in relatively little increase in carcinogenicity (e.g. m-toluidine) or no increase (e.g. m-phenylenediamine).

2. Introduction of a chlorine atom at the para position usually decreases or eliminates carcinogenicity for rats, though not for mice.

3. Introduction of a fluorine atom at the para position (as in 4-fluoroacetamide or tetrafluoro-m-phenylenediamine) leads to a small increase in carcinogenicity in mice, probably because the ring positions usually involved in detoxification are blocked.

TABLE 3.4.2

CARCINOGENIC MONOCYCLIC AROMATIC AMINES

SUBSTITUENTS	COMPOUNDS	CARCINOGENICITY DATA
(a) Monoamines		
R=H	- aniline	o - 2 - Va, MO
R=H, 2=Cl, 4=Cl, 6=Cl	- 2,4,6-trichloroaniline	o - 1(male) - Va, ?Li
R=H, 2-CH_3	- o-toluidine	o - 1, 2 - Cs, Va, MO
R=H, 3=CH_3	- m-toluidine	o - 1,(male) - ?Li
R=H, 4=CH_3	- p-toluidine	o - 1 - Li
R-H, 2=CH_3, 4=CL	- 4-chloro-o-toluidine	o - 1 - Va
R=H, 2=CH_3, 4=CH_3	- 2,4-xylidine	o - 1(female) - Lu; o - 2 - Sc
R=H, 2=CH_3, 5=CH_3	- 2,5-xylidine	o - 1,2 - Sc, Va; o - 2 - Li, ?Sc
R=H, 3=CH_3, 4=CH_3	- 3,4-xylidine	? - 2 - ?Pi
R=H, 2=CH_3, 4=CH_3, 5=CH_3	- 2,4,5-trimethylaniline	o - 1 - Li, Lu, MO
R=H, 2=CH_3, 4=CH_3, 6=CH_3	- 2,4,6-trimethylaniline	o - 1,2 - Li, Lu, Va, MO
R=$COOCH_3$, 4=F	- 4-fluoroacetanilide	? - 2 - ?Pi
(b) Diamines		
R=H, 2=NH_2	- o-phenylenediamine	o - 1,2 - Li
R=H, 3=NH_3, 6=CH_3	- 2,4-toluenediamine	o - 2 - Li, Sc, MO
R=H, 3=NH_2, 2=F, 4=F, 6=F	- tetrafluoro-m-phenylene-diamine	o - 1(male) - Li

Note: m-Phenylenediamine and p-phenylenediamine has not been adequately tested(9).

4. Introduction of a second amino group ortho to the NH_2 group in aniline (but not at the meta or para positions) enhances carcinogenicity.

5. The carcinogenicity of chloronitrobenzene compounds appears to parallel that of the chloroanilines. This would be expected since the nitro compounds are converted first to the corresponding hydroxylamines, then to the anilines, by nitro reductase enzyme systems in the body.

6. The carcinogenicity of the N-hydroxy derivatives of aniline has not been sufficiently tested to establish their possible carcinogenic effects.

3.4.3 Biphenylamines

(a) Monoamino Biphenyls

As indicated earlier, 4-aminobiphenyl has been found to be carcinogenic to men who were occupationally exposed. The results of extensive experimental testing of monobiphenyl derivatives are tabulated in Table 3.4.3.

Generalizations relating to the carcinogenicity of the monoamine biphenyl compounds which can be drawn from an inspection of the table, and from findings reported in the literature, include:

1. Carcinogenicity is moderately enhanced when the amino group is para to the biphenyl bond. When the amino group is in the 2 or 3 position, carcinogenicity is reduced.

2. Substitution of a methyl group ortho to the amino group often enhances carcinogenicity. Substitution of the methyl group in the meta (2 or 2') position reduces or

TABLE 3.4.3

CARCINOGENIC MONOAMINO BIPHENYLS

SUBSTITUENTS	COMPOUNDS	CARCINOGENICITY DATA
R_1=H, R_2=H	- 4-aminobiphenyl* (see Note 1)	o - 1 - Li; o - 2 - ?Li, ?I, Br; o - 3,5 - Bl
R_1=H, R_2=OH	- 4-biphenylhydroxylamine	s.c. - 1 - Li
R_1=H, R_2=$COCH_3$	- 4-biphenylacetamide	o - 2 - A, I, Br
R_1=OCH_3, R_2=$COCH_3$	- N-acetoxy-4-biphenylacetamide	s.c. - 2 - Lo
R_1=CH_3, R_2=CH_3	- 4-biphenyldimethylamine	o - 2 - A, I, Br
R_1=OH, R_2=$COCH_3$	- 4-biphenylacethydroxamic acid	o - 2 - A, Br, Lo
R_1+R_2=O	- 4-nitrobiphenyl	o - 5 - Bl
R_1=H, R_2=H, 2=CH_3 or F	- 2-methyl- (or 2-fluoro-)-4-phenylaniline (see Note 2)	o - 2 - A, I, (Br)
R_1=H, R_2=H, 3=OCH_3	- 3-methoxy-4-biphenylamine	s.c. - 2 - Bl
R_1=H, R_2=H, 3'=F	- 3'-fluoro-4-phenylaniline	o - 2 - Br
R_1=H, R_2=H, 4'=F	- 4'-fluoro-4-phenylaniline	o - 1 - Li; s.c. - 2 - Ki, Li, I, Pa
R_1=H, R_2=H, 3=CH_3, 2'=CH_3	- 3,2'-dimethyl-4-biphenylamine	s.c., o - 2 - Bl, Br, A, I, SG
R_1=H, R_2=H, 3=CH_3, 3'=CH_3	- 3, 3'-dimethyl-4-biphenylamine	s.c. - 2 - I, SG
R_1=H, R_2=H, 3=CH_3, 2'-CH_3, 5'=CH_3	- 3,2',5'-trimethyl-4-biphenylamine	s.c. - 2 - Li, I
R_1=H, R_2=H, 3=CH_3, 2'=CH_3 4'=CH_3, 6'=CH_3	- 3,2',4',6'-tetramethyl-4-biphenylamine	s.c. - 2 - Li, I

Note 1: 2-aminobiphenyl is not carcinogenic

Note 2: 2'-methyl-4-phenylaniline is not carcinogenic
3-methyl-4-phenylaniline is not carcinogenic
2-chloro-4-phenylaniline is not carcinogenic

eliminates the carcinogenic effect. The effect of ortho substitution of a group other than methyl (e.g. Cl or OH) produces varied carcinogenic responses.

3. Substitution of an F atom in a ring position, particularly at the 4' or para position relative to the diphenyl bond, enhances carcinogenicity since it blocks ring hydroxylation which is believed to be a detoxification mechanism.

4. N-hydroxylation increases carcinogenicity, and is believed to be the first metabolic step in the carcinogenic activation of the aromatic amines.

5. There is a possibility that conversion of the arylhydroxylamines to nitroso compounds, which can take place readily under biological conditions, may be an important metabolic pathway in the activation of aromatic amine compounds, at least in some animal species.

(b) Diamino Biphenyls

The carcinogenic effect of benzidine on the urinary bladder in man has been mentioned previously. A number of benzidine derivatives have been found carcinogenic in animals, as tabulated in Table 3.4.4.

Among the few generalizations which can be drawn with respect to the carcinogenic effect of various substituent groups in the basic diaminobiphenyl molecule are:

1. N,N'acetylation induces carcinogenicity in the liver and other organs in rodents.

2. Ortho substitution of CH_3, OCH_3 and COOH groups and of Cl atoms (at the 3,3' positions) produces compounds which are all carcinogenic. On the other hand, substitution of OH groups at these positions eliminates carcinogenicity.

3. There is no evidence either to support or to contradict the role of N-hydroxylation as a first step in the metabolic activation of benzidine or its derivatives.

3.4.4 Extended Diphenylene Amines

As indicated earlier, methylenedianiline has not been found to be carcinogenic in man, but it is possibly carcinogenic to rats. There is epidemiological evidence for believing that the dye auramine is a bladder carcinogen to man.

In Table 3.4.5 which shows the derivatives of methylenedianiline, and of other extended diphenylene amine derivatives that have been found to be carcinogenic, we have not included the stilbeneamines, which have a -CH=CH- group in the X position. In this tabulation, the "X" functionality is the group between the aromatic rings. Many stilbeneamine derivatives are carcinogenic to the rat and at least two to the mouse. Clayson and Garner(5) give a fairly recent listing of these amines.

From the review of Table 3.4.5 and of reports in the literature, the following generalizations may be drawn regarding the carcinogenicity of the extended diphenylene amines.

1. The group linking the phenyl rings in carcinogenic derivatives may be $-CH_2-$, -CH=CH-, -CNH-, -O-, or-S-.

2. Among the methylenedianiline derivatives, the 3,3'-methyl and 3,3'-chloro derivatives (ortho to the amino groups) are carcinogenic.

3. Substitution of a Cl atom at the 3,3' positions in 4,4'-diaminodiphenylether also gives a carcinogenic derivative.

4. Simple amino derivatives in which the amino group is para to the extended phenyl linkage may also be carcinogenic, e.g. 4-phenylthioacetanilde.

5. The metabolic pathways involved in the carcinogenic activation of the extended diphenylene amines do not appear to have been established.

3.4.5 Fused Aromatic Ring Amines

Consideration of the fused aromatic ring amines has been limited in this report to the naphthylamines and their derivatives. This limitation has resulted in the omission of reference to the fluorenyl amines, which are probably the most thoroughly investigated of all the aromatic amines, and of the anthramine and phenanthramine derivatives. For a review of the carcinogenicity of these series, see Clayson and Garner(5).

beta-Naphthylamine and its dichloroethyl derivative have both been found carcinogenic to the bladder in man. Other naphthylamines which have been found carcinogenic to animals are tabulated in Table 3.4.6.

The following generalizations may be drawn regarding the carcinogenicity of the naphthylamine derivatives:

1. The derivatives of beta-naphthylamine tend to have greater carcinogenicity than do the alpha-naphthylamine derivatives.

2. Carcinogenicity is associated with N-substitution, in contrast to ring-substitution.

3. The first step in the carcinogenic activation of naphthylamine compounds is believed to be the formation of N-hydroxylamines. This is followed by esterifi-

TABLE 3.4.4

CARCINOGENIC DIAMINO BIPHENYLS (BENZIDINES)

SUBSTITUENTS	COMPOUNDS	CARCINOGENICITY DATA
R=H	benzidine*	o - 5 - Bl; o - 4 - Li; s.c. - 1,2 - Li, I, A
R=H, 3=CH_3, 3'=CH_3	- o,o'-toludine*	s.c. - 2 - A, Br, Lo, Ly, Sk
R=H, 3=OCH_3, 3'=OCH_3	- o,o'-dianisidine	o - 4 - St
R=H, 3=COOH, 3'=COOH	- 3,3'-benzidine dicarboxylic acid	s.c. - 2 - Br, ?Li, Va
R=H, 3=Cl, 3'=Cl	- 3,3'-dichlorobenzidine	o, s.c. - 2 - Bl, Br, A, I, Ly, Sk; o - 4 - Bl, Li, Bo
R=$COCH_3$	- N,N'-diacetylbenzidine	o - 2 - Br, A, Li
R=$COCH_3$, 2=CH_3	- 2-methyldiacetylbenzidine	o - 2 - Br, A, I

Note: 3,3'-dihydroxybenzidine is not carcinogenic

TABLE 3.4.5

CARCINOGENIC EXTENDED DIPHENYLENE AMINES

SUBSTITUENTS	COMPOUNDS	CARCINOGENICITY DATA
X=CH_2, R=H	- methylenedianiline (?)	o, s.c. - 2 - ?Li
X=CH_2, R=H , 3=CH_3, 3'=CH_3	- 4,4'-bis(2-o-toluidine)	o - 2 - Li, Lu, Br, Sk
X=CH_2, R=H , 3=Cl, 3'=Cl	- 4,4'-bis(2-chloroaniline)	o - 2 - Li, Lu; o - 1 - Li, Va
X=CNH, R=$(CH_3)_2$	- auramine*	o, s.c. - 2 - Lo, Li, ?I; o - 1 - Li
X=O, R=H	- 4,4'-diaminodiphenyl ether	o, s.c. - 1,2 - Li, MO
X=O, R=H , 3=Cl, 3'=Cl	- 3,3'-dichloro-4,4'-diamino-diphenyl ether	s.c. - 2 - A
X=S, R=H	- 4,4'-dithioaniline	o - 2 - Br
X=NH, R=H , 4'=H	- 4-aminodiphenylamine (see Note 1)	

Note 1: In 4-aminodiphenylamine the NR group at the 4' position has been replaced by a hydrogen atom; the product does not appear to be carcinogenic.

TABLE 3.4.6

CARCINOGENIC FUSED AROMATIC RING AMINES

SUBSTITUENT	COMPOUND	CARCINOGENICITY DATA
R=H	- 2-naphthylamine*	o - 1 - Li; o - 4,5,6 - Bl; s.c. - 5 - Bl
R=H , 1=OH	- 2-amino-1-naphthol	bl - 1 - Bl
R-H , 1=OCH_3	- 1-methoxy-2-naphthylamine	s.c. - 1 - I
R=H , 3=CH_3	- 3-methyl-2-naphthylamine	o, s.c. - 2 - Br, Sk, I, Lo, ?Ki
R=OH	- 2-naphthylhydroxylamine	sk - 1 - Lo; i.p. - 2 - Lo; bl - 5 - Bl; s.c. - 1 - Li, Lu
R=$(CH_2-CH_2-Cl)_2$	- N,N-bis(2-chloroethyl)-2-naphthylamine*	i.p. - 1 - Lu
R= -NO	- 2-nitrosonaphthylamine	i.p. - 2 - Li; s.c. - 1(male) - Li, Lu
1=NHOH, 2=H	- 1-naphthylhydroxylamine	sk - 1 - Lo; o - 2 - Lo; i.p. - 2 - Li, Lu; s.c. - 1 - Li, Lu

cation and/or nitroso formation. The former is probably the most important pathway to induce carcinogenicity in those animal species which can acetylate aromatic amines. In dogs, the formation of nitroso derivatives appears to play a role in the production of the ultimate carcinogens.

3.4.6 Aromatic Azo Compounds

The very large number of aromatic azo compounds which have been found to exhibit carcinogenic activity make it very difficult to isolate more than a few structural features which are apparently related to carcinogenicity. From a review of the literature, the following generalizations can be substantiated.

1. The azo bond is essential to the carcinogenic effect of some of these compounds, since cleavage of the azo bond in these compounds results in products which are not carcinogenic.

2. The presence of at least one N-methyl group appears essential for carcinogenicity of the aminoazobenzenes in rats. N-disubstitution of ethyl, n-propyl, n-butyl and n-amyl groups does not induce carcinogenic activity.

3. Ring-substitutions by -OH groups at the 2, 3, 2', 3' and 4' positions, and by $-NO_2$, $-NH_2$, $-SO_3H$ and -COOH groups at the 4' position, eliminate the carcinogenicity of N,N-dimethyl-p-phenylazoaniline.

3.5 ENVIRONMENTAL TOXICOLOGY

3.5.1 Aromatic Amines

There is a general dearth of published data concerning the effects of aromatic amines in the natural environment. Most of the available information describes laboratory studies, which investigate the effects of high dose levels of these compounds on the physiology and biochemistry of test organisms(25).

Aromatic amines have been shown to induce cancer in laboratory animals(26,27,28). It is not clear, however whether these high dose laboratory studies reflect environmental conditions, where concentrations are believed to be generally low.

Aquatic Biota

Aromatic amino compounds, in general, appear to be acutely toxic to fish(29). The toxicity of thirty-four dye stuffs derived from aromatic amines is listed in Table 3.5.1. Toxicity is expressed in terms of a "critical range", which is defined as the range of concentration in mg/L, below which all fish live for 24 hours and above which all die.

The toxicity of these amines was tested with creek chub (Semotilus Atromaculatus), a fish considered to be average tolerance when found in well aerated water(30).

A number of these compounds displayed critical concentrations as low as 5 mg/L, while some had relatively high values. A majority of compounds were in the 20-80 mg/L range. These concentrations relate to acute toxicity limited by death. Chronic or sublethal effects could be expected to occur at considerably lower concentrations.

The maximum allowable concentration of aniline in drinking water has been given as 5.0 mg/L.(31) A wide range of toxic levels has been reported for fish; 100 mg/L for trout, 200 mg/L for minnows and 1000 mg/L for goldfish (Carassius Auratus)(32). Aniline killed sunfish (Lepomis Sp.) in one hour at concentrations of 1020-1120 mg/L(33). Concentrations as low as 250 mg/L are reported to be deadly to fish(34).

Lower organisms, such as algae and zooplankton, are affected by a wide range of aniline concentrations. For example, the threshold concentration for immobilization of Daphnia Magna during prolonged exposure in Lake Erie water was 179 mg/L(35). In contrast, the median threshold effect toward Daphnia Sp. occurred at 0.4 mg/L during a two day exposure(36). (The "median threshold effect" refers to the concentration at which 50% of the test animals are affected at the end of the experimental period.) The differences in toxic levels may be a function of the experimental design, or perhaps the analytical technique.

In a four day exposure, the median threshold effect occurred at 10 mg/L for the algae, (Scenedesmus)(36). Studies with blue-green algae (Agmenellum Quadruplicatum) showed that this species was very sensitive to aniline and p-toluidine(37). Growth was inhibited by approximately 1 mg/L of p-toluidine. Seven other species of blue-green algae showed varying sensitivities to concentrations ranging from 1-100 mg/L of p-toluidine.

Approximately 0.5 mg/L of p-toluidine was needed to inhibit green algae, a diatom and two species of bacteria(37). This observation is in contrast to those which have demonstrated that the bacterium (Escherichia Coli) was not affected by aniline concentrations as high as 1000 mg/L(36).

It is known that aniline can undergo biological N-methylation, acetylation, and hydroxylation in different phases of a model ecosystem(39). The results of some experimental work(38) with activated sludge suggest that benzidine does not undergo the same transformations.

It appears that the aromatic amines, in general, can be biologically transformed, although it is uncertain as to the degree to which biodegradation proceeds(38).

The modes of toxicity of aromatic amines in terrestrial vertebrates are well documented(40,41,42,43). However, there is a definite lack of such information for their aquatic counterparts. If one assumes that aquatic vertebrates have physiological responses similar to those of terrestrial vertebrates, then the response of fish and amphibians to aromatic amines may be said to be similar to those of humans, dogs, rabbits, birds, etc. Consequently, vertebrates exposed to aromatic amines in the aquatic environment may suffer the effects of mutagenesis, carcinogenesis and methaemoglobinaemia as do terrestrial vertebrates when exposed to these compounds.

Algae are the primary producers of biomass in an aquatic ecosystem. If this primary production is reduced, inhibited or adversely affected in any way, the effects are generally observed at all trophic levels of the ecosystem. Since even very low concentrations of some aromatic amines affect algae, it is clear that their presence can affect the entire ecosystem.

Terrestrial Biota

There is an adequate amount of evidence which suggests that different vertebrates exhibit similar responses when exposed to aromatic amines(25,26,27,40,41,42,43). It appears that

regardless of the mode of exposure, the toxicological consequences of aromatic amines to humans are similar to those observed among other mammals.

Aromatic amines induce ferrihaemoglobin formation in birds and mammals. There is also evidence that they cause the formation of methaemoglobin which effectively reduces the oxygen carrying-capacity of the blood. Consequently, organisms may expire from anoxia, if the concentration of methaemoglobin is sufficiently high(41,42).

Aniline was toxic to all the mammals tested with the compound, including humans(38,41). The LD_{50} for rats and dogs following oral administration is 400 and 500 mg/kg respectively(25). Aniline absorbed by the skin is also toxic(25). As described above, the toxic action of aniline is due to the formation of methaemoglobinaemia, with the resultant loss in efficiency of oxygen transport(41).

At present, there is no evidence to suggest that aniline is bioaccummulated by plants and animals. Animals probably have a limited capacity for accummulating aniline, as its metabolites have been observed in the urine of various animals(25,43).

Aniline may enter plants through their roots, however it is also possible for exposure to occur from fallout from the atmosphere. The mechanisms of atmospheric deposition include adsorption onto particulate matter, gravitational settling and rain washout.

Once deposited on the photosynthetic and respiring surfaces (leaves and their analogues), aniline might exert its toxic effect by disturbing photosynthetic or respiration physiology. Aniline may reach a photochemically excited state followed by energy release, which could be harmful to

plants(44). Some of the consequences of air-deposited aniline may be partial leaf destruction and/or defoliation. Aniline that is deposited into soils may exert its effects by producing growth aberrations or interfering with germination.

Benzidine and some of its metabolites are excreted in the urine of exposed mammals(25,43). Mammals may also absorb benzidine through the lungs or from the digestive system. Dose levels of about 200-300 mg/kg are known to induce death in mice.

Very little information is available for the aromatic amine compounds: 4-aminobenzidine, 3-3'-dichlorobenzidine, ortho-toluidine, ortho-dianisidine, naphthylamine, phenylene-diamine or methylenedianiline. These compounds however, are similar to each other in that they are carcinogenic to man and other animals(25).

3.5.2 Azo Dyes

Azo dyes are known to be toxic to certain bacteria, aquatic organisms and plant life(29).

The use of dyes dates back to at least the stone age, but despite the long history of usage, the list of the known effects on living organisms is not extensive(47).

Aquatic Biota

Direct, acid and basic dye wastes are all highly coloured and commonly have a higher biological oxygen demand (BOD) than that of domestic sewage(48).

Direct dyes are readily soluble and can be used without a mordant. However, where mordants and adjuvants are employed, they may prove to be more toxic that the dye itself(49).

The high BOD of direct dye waste streams may have some environmental significance if dissolved oxygen is depleted in surface waters. For example, fish such as salmonids (trouts, chars and salmon), pickerel and a number of other species have low tolerance to low dissolved oxygen(50).

The presence of organic compounds interferes with natural stream processes. They may decrease the effectiveness of algae-bacterial treatment systems by inhibiting photosynthetic oxygenation(51).

Some work has been conducted which investigated the toxicity and accummulation of various dye compounds in three species of fish(47,55). The dyes tested belonged to the following classifications: disperse, direct, acid, base, sulfur and fluorescent.

The fathead minnow (Pimephales Promelas) was used in 96-hour bioassays to determine the toxicity of 46 dyes(49). The LC_{50}, or the concentration at which 50% of the experimental animals survive 96 hours, was estimated by interpolation for each dye. A complete listing of the dyes and the toxicity is shown in Table 3.5.1. Also shown in this table are the colour index number and name of each dye.

The LC_{50} values for 29 of the dyes tested are higher than 180 mg/L, 3 others fell between 100 and 180 mg/L and the remaining 14 were lower than 100 mg/L(47).

The effects of dyes on the growth of bacteria have been studied. The basic aminotriphenylmethane dyes, brilliant green and malachite green, inhibited growth of 26 and 10 bacterial species respectively(39). The basic triaminotriphenylmethane dyes were inhibitory as follows: crystal violet, 27 species; basic fuchsia, 16; p-rosaniline, 19; methyl green, 18; methyl violet, 24. The basic dyes appear to be more inhibitory to bacterial growth than were acid and neutral dyes(56).

The toxicity of fluorescent whitening agents (FWA) was studied on bluegill (Lepomis Macrochiras) and channel catfish (Ictalurus Punctatus)(55). FWA's are dyestuffs that have been used for many years at low levels (up to 0.7% total FWA) in soap and detergent products. They can be considered dyes even though they appear white to the human eye.

FWA's have been found in the flesh of fish caught downstream from an outfall discharging treated sewage containing this material(58). The results of a laboratory test showed that FWA was accummulated in the fatty tissue of goldfish (Carassius Auratus) to levels 1000 times above that in the surrounding water(57,58). When transferred to clean water, however, accummulations of this compound were rapidily eliminated.

The acute toxicity of FWA's to bluegill ranged from 26-1000 mg/L. An obvious distinction was apparent between the accummulation of the nonionic and anionic FWA's in bluegill and channel catfish.

TABLE 3.5.1

TOXICITY OF SELECTED DYES TO THE FATHEAD MINNOW, PIMEPHALES PROMELAS AND COMPARISON OF TL_{50} TO CONCENTRATIONS PRODUCING COLOUR

Dye Class	CI #	Dye	TL_{50}, mg/l			Temp.	Concentration, mg/l to Produce Colour		
			24 hr.	48 hr.	96 hr.	C	50 APHA	100 APHA	150 APHA
Nitro	10338	Disperse Yellow 42	>180	>180	>180	15	7.8	16.5	25.2
Monoazo	11855	Disperse Yellow 3	>180	>180	>180	15	2.9	6.1	9.3
	14645	Merdant Black 11	10.0	6.0	6.0	15	0.3	0.9	4.4
	15510	Acid Orange 7	>180	>180	165	17	0.3	0.7	1.0
	15711	Acid Black 52	7.0	6.2	6.2	15	1.2	2.3	3.4
	18965	Acid Yellow 17	>180	>180	>180	17	0.7	1.4	2.2
	19555	Direct Yellow 28	>180	180	>180	15	0.8	1.5	2.2
		Acid Yellow 151	29	29	29	15	0.6	1.0	1.5
Diazo	20170	Acid Orange 24	>180	>180	130	17	0.2	0.5	0.7
	20470	Acid Black 1	>180	>180	>180	15	0.3	0.6	0.9
	21010	Basic Brown 4	> 10	7.5	5.6	20	0.35	0.7	1.1
	22610	Direct Blue 6	>180	>180	>180	17	0.4	0.9	1.3
	24401	Direct Blue 218	>180	>180	>180	17	0.4	0.8	1.4
	24890	Direct Yellow 4	>180	>180	>180	15	0.2	0.4	0.7
	24895	Direct Yellow 12	>180	>180	125	15	0.3	0.6	1.1
	25135	Acid Yellow 38	24	24	23	15	0.9	2.0	3.3
	26360	Acid Blue 113	4.5	4.5	4.4	15	0.4	0.8	1.2
	28160	Direct Red 81	>180	>180	>180	17	0.3	0.5	0.8
	29025	Direct Yellow 50	>180	>180	>180	17	0.6	1.5	2.3
	29160	Direct 23	>180	>180	>180	17	0.6	1.2	1.8
Polyazo	30145	Direct Brown 95	>180	>180	>180	17	0.4	0.7	1.1
	30235	Direct Black 38	>180	>180	>180	17	0.4	0.9	1.5
	31600	Direct Black 80	>180	>180	>180	17	0.2	0.3	0.5
Stilbene	40000	Direct Yellow 11	>180	>180	>180	17	0.4	0.8	1.3
	40622	Fluroescent Brightening Agent 28	>180	>180	>180	17	-	-	-
		Direct Yellow 106	>180	>180	>180	17	0.5	1.0	1.9

TABLE 3.5.1 (cont'd)

Dye Class	CI #	Dye	TL_{50}, mg l			Temp. C	Concentration, mg/l to Produce Colour		
			24 hr.	48 hr.	96 hr.		50 APHA	100 APHA	150 APHA
Di- and Tri-phenylmethane	42000	Basic Green 4	> 0.2	0.12	0.12	18	0.1	0.3	0.4
	42535	Basic Violet 1	0.21	0.13	0.047	15	0.1	0.2	0.3
Quinoline	47020	Disperse Yellow 54	>180	>180	>180	15	4.9	9.9	14.9
Polymethane	48055	Basic Yellow 11	4.4	4.0	3.2	18	0.3	0.6	0.9
Oxazin	51005	Basic Blue 3			4.0	15	0.1	0.3	0.4
Thiazin	53185	Sulfur Black 1	>180	>180	>180	15	7.8	16	23
	53630	Vat Blue 43	>180	>180	>180	15	3.2	6.4	9.5
Anthraquinone	59105	Vat Orange 1	>180	>180	>180	15	5.2	12.2	19.2
	59825	Vat Green 1	>180	>180	>180	15	6.7	13.4	20.0
	61505	Disperse Blue 3	> 1	> 1	1	15	2.0	4.0	6.1
	61570	Acid Green 25	> 10	5.7	6.2	18	0.9	1.8	2.7
	62055	Acid Blue 25	12.5	12.5	12	15	0.5	1.0	1.5
	62500	Disperse Blue 7	>180	142	52	15	2.5	5.0	7.5
	63010	Acid Blue 45	>180	>180	>180	15	0.5	1.0	1.5
	67300	Vat Yellow 2	>180	>180	>180	15			
	69015	Vat Brown 3	>180	>180	>180	15	9.5	18.5	28.3
	69500	Vat Green 3	>180	>180	>180	15	16.5	34.5	57
	69825	Vat Blue 6	>180	>180	>180	15	8.5	18	28
		Disperse Red 60	>180	>180	>180	15	3.1	6.2	9.4
Phthalocyanine	74180	Direct Blue 86	>180	>180	>180	17	0.6	1.3	2.0

IMPORTANCE OF AROMATIC AMINES AND AZO DYES IN ONTARIO

4

4.1 AROMATIC AMINES

4.1.1 Introduction

Available information indicates that none of the "primary group amines" is manufactured in Ontario. Usage of primary group amines in Ontario is limited to only a few industries, as presented in Table 4.1.1. The overall quantities, with the exception of aniline, appear to be small.

The primary industries concerned with the use of these materials are the following: rubber, consumer hair dyes, photo, pigments, plastics and epoxies, gasoline, agricultural chemicals, pharmaceuticals, and isocyanate production.

4.1.2 Rubber Industry

The primary use of aromatic amines in this industry is in the production and use of rubber stabilization chemicals. These are usually antioxidants or antiozonants.

The important rubber antioxidants may be divided chemically into two classes: amines and their derivatives; phenols and their derivatives. The power, as antioxidants, of members of each class is approximately the same, but essential differences lie in their effectiveness in the presence of carbon black and in the degree of staining imparted to vulcanizates on exposure to light.

Consequently, the amines are used mostly in darker coloured rubbers where staining is not a problem. Conversely, the phenolics are used more in lighter coloured rubbers where aesthetics are more important.

Consumer exposure to amine stabilizers will come from contact with auto tires, V-belts and rubber hoses, foam rubber carpet backings, various sponge goods, padding, sporting goods and shoes.

Normally the stabilizer is added in concentrations of from one to three per cent by weight. Considering the variety of applications of rubber listed above, the likelihood of the consumer being exposed to these materials is high.

In Ontario, the major aromatic amine feedstock for rubber chemicals is di-phenylamine, which is used at a rate of approximately three million pounds annually. Of the primary group amines, aniline is consumed at a rate of approximately two million pounds per annum; para-nitroaniline is consumed at an annual rate of approximately one hundred thousand pounds. The resulting products, selections of which are presented in Table 4.1.2, and illustrated in Figure 4.1.1. total approximately four million pounds per year.

TABLE 4.1.1

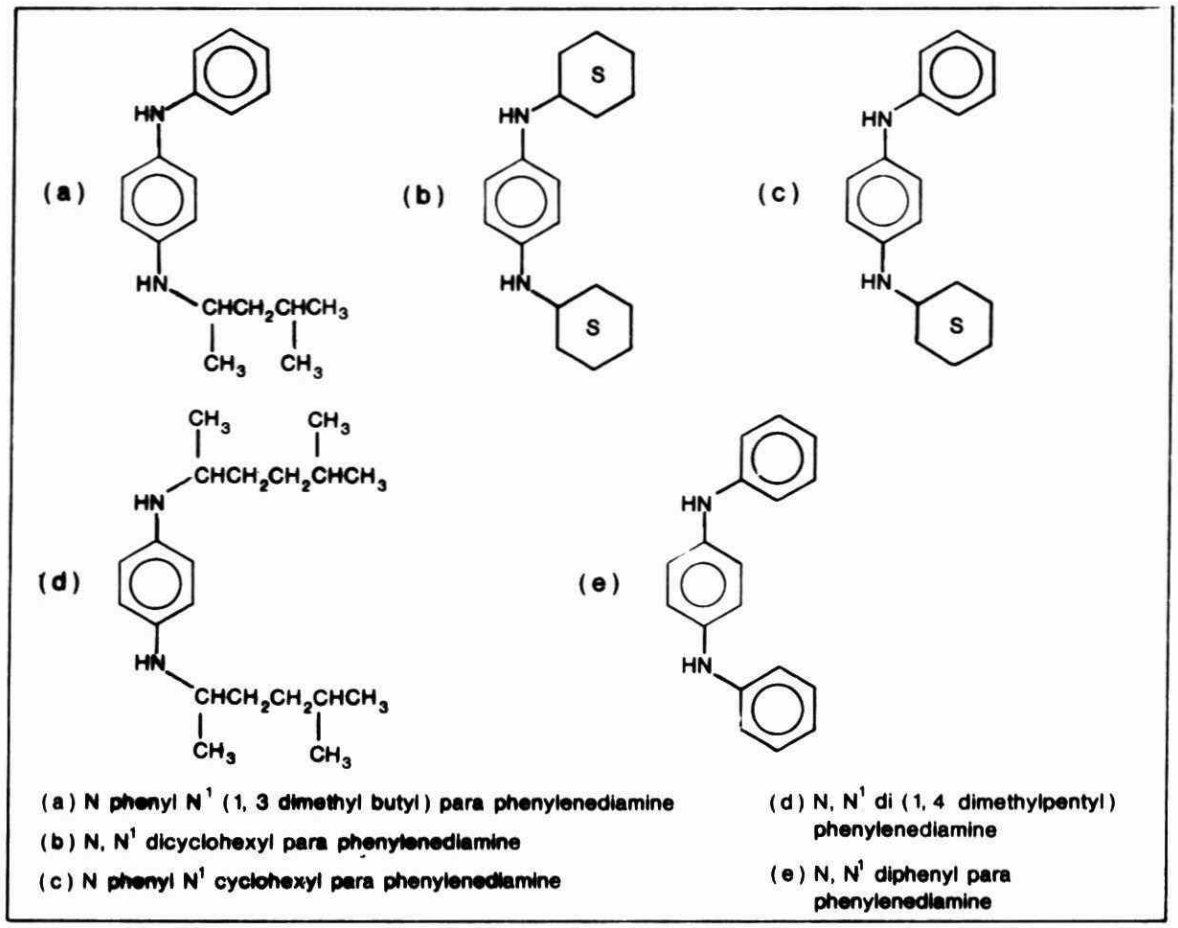
USE OF PRIMARY GROUP AMINES IN ONTARIO

Anilines	:	manufacture of rubber chemicals
	:	hardeners in industrial epoxies
	:	corrosion inhibitor
Total use:	approx. 2 million lbs/year	
Phenylenediamines	:	consumer hair dyes
	:	hardener in industrial epoxies
	:	photographic developer
Total use:	no statistics available	
Benzidines	:	manufacture of pigments
Total use:	approx. 150 000 lbs/year	
Methylenedianilines	:	hardener in industrial epoxies
	:	miscellaneous
Total use:	approx. 50 000 lbs/year	
Naphthylamines	:	rubber antioxidants, accelerators
	:	polyolefin antioxidants
Total use:	No statistics available, believed to be small. Being withdrawn from markets	

TABLE 4.1.2

RUBBER CHEMICALS PRODUCED AND USED IN ONTARIO
(Listed in order of importance)

(a) N-phenyl-N'-(1, 3 dimethylbutyl)-para-phenylenediamine
(b) N-phenyl-N'- isopropyl-para-phenylenediamine
(c) 4, 4'-bis-(α, α Dimethylbenzyl)diphenylamine
(d) N, N'-di-sec-butyl-para-phenylenediamine
(e) N-nitrosodiphenylamine
(f) N, N', dicyclohexyl-para-phenylenediamine
(g) Condensation products of diphenylamine and acetone (solid)
(h) N-phenyl, N', Cyclohexyl-para-phenylenediamine
(i) N, N', diphenyl-para-phenylenediamine
(j) N, N', bis (1, 4 dimethyl pentyl) para phenylenediamine



(a) N phenyl N^1 (1, 3 dimethyl butyl) para phenylenediamine
(b) N, N^1 dicyclohexyl para phenylenediamine
(c) N phenyl N^1 cyclohexyl para phenylenediamine
(d) N, N^1 di (1, 4 dimethylpentyl) phenylenediamine
(e) N, N^1 diphenyl para phenylenediamine

Figure 4.1.1 SELECTED EXAMPLES OF RUBBER CHEMICALS

Napthylamines have been identified as rubber chemicals, but no statistics on their usage in Ontario have been uncovered. Generally, it seems that these materials have been superseded by more effective and less hazardous compounds.

Statistics Canada reports that an additional two million pounds of various rubber chemicals were imported into Canada in 1976. The major proportion of these are probably destined for Ontario.

Only two manufacturers of rubber chemicals in Ontario have been identified. These processes are localized in single plant operations in smaller communities and as such can be considered point sources. These operations are discussed in more detail in a later chapter.

The rubber chemicals are transferred to a number of appropriate consuming manufacturers, where they are blended to produce the desired product.

The potential for emission under these circumstances is greater, in that the consuming manufacturers are far greater in number and of broader distribution throughout the province.

Perhaps the greatest source for release into the environment comes from the actual end products. For example, the rubber portion of an auto tire may have 3% by weight aromatic amine compounding chemicals. As the tire wears out through use, the rubber and its constituent aromatic amines will be broadly distributed throughout the environment as a fine dust. A brief discussion of rubber dissipation in the environment is presented in the Appendix.

4.1.3 Hair Dyes

This section is quoted for the most part from an excellent review article authored by Marzulli.(1)

The most common dyeing systems for colouring the hair (Table 4.1.3) are the permanent (oxidation) hair dyes, lasting for several months, the semi-permanent (non-oxidation) hair dyes, which last up to five weeks; and the temporary (non-oxidation) hair dyes, which can be rubbed off or removed with shampooing. Metallic hair dyes contain lead acetate; and vegetable hair-colouring products contain henna, which is receiving renewed attention because of a trend toward more natural hair colouring.

Most hair dyes sold in the United States and Canada are the oxidation type. They are usually compounded of seven to twelve aromatic substances (intermediates), some of which act as couplers. Others convert to coloured substantive compounds on oxidation and polymerization in alkaline solution.

The couplers are generally meta-aromatic diamines, hydroxyamines, and diphenols, which are not themselves oxidized, but which condense with the benzoquinone-imine derivatives that form in the oxidizing hair mixture. The intermediates are present at 0.1 to 4 percent concentration in an ammoniacal base usually containing a detergent and a sequestering agent. The intermediates are diluted and oxidized by mixing with equal parts of 6 percent hydrogen peroxide. This process may bleach the natural hair pigment.

Examples of intermediate aromatic amines used in these preparations are listed in Table 4.1.4.

Semi-permanent dyes penetrate and dye the hair directly, without oxidation. Some of the preparations used for semi-permanent colouring contain "1,2-metal complex dyes" with solubilizing groups, exemplified by the Irgalan, Cibalan, or Ortolan range of dyes. Others contain toluenediamine or anthraquinone dyes or solvent-assisted nitro, disperse, and azo dyes. Certain oxidation colours are used as the main colouring components, but without an oxidizing agent. Among these are nitro compounds, such as 2-nitro-1,4-phenylenediamine, 4-nitro-1,2-phenylenediamine, and 4-nitro-2-aminophenol.

Finally, there are N-substituted derivatives of nitrophenylenediamines and nitroaminophenols in which one to four alkyl and/or hydroxyethyl or related groups replace the hydrogen of the amino or phenol groups of the nitrophenylenediamines or nitroaminophenols.

Temporary dyes consist of:

(a) mixes of Food, Drug and Cosmetic (FD&C) colours with citric acid
(b) mixtures of basic dyes such as methylene blue, fuchsin and methyl violet
(c) salts or complexes formed by dyes with a cationic detergent, and
(d) colouring shampoos containing FD&C or external D&C dyes dissolved in a shampoo base.

Recently dyes based on lead acetate have become popular, especially with males for darkening grey hair. These products usually contain the dissolved lead salt and elemental sulfur. After application to hair and subsequent exposure to air, the ionic lead reacts with the sulfur to form a mixture of insoluble sulfides and oxides imparting a darker colour. Since the colouring is gradual, they are also called progressive hair dyes. Bismuth citrate is also used in some hair dyes.(1)

There appears to be no production of hair dyes in Ontario. Evidently, they are manufactured in Quebec and then distributed in Ontario.

The only apparent source of emission into the environment in Ontario occurs during consumer use. Since in the original solution, the formulation may contain only about 4% aromatic amines, and some of this will be absorbed into the hair, the final concentration of amines in discharge waters will probably be low.

TABLE 4.1.3

TYPES OF HAIR DYES*

Permanent (oxidation) hair dyes - last several months	
Examples:	Colour Silk (Revlon)
	Miss Clairol (Clairol, Inc.)
	New Dawn (Alberto Culvert)
	Preference (L'Oreal)
	Tried and True (Max Factor)
Semi-permanent (non-oxidation) hair dyes - last up to 5 weeks	
Examples:	Loving Care (Clairol, Inc.)
	Nice Change (Roux)
Temporary (non-oxidation) hair dyes - removed by rubbing or shampooing	
Examples:	Come Alive (Clairol, Inc.)
	Fanciful Rinse (Roux)
Metallic hair dyes (contain lead acetate)	
Examples:	Grecian Formula (Combe, Inc.)

* The examples given in each category account for approximately 85% of sales

TABLE 4.1.4

AROMATIC AMINES IN HAIR DYES

Some Aromatic Amines used in permanent hair dyes by shade produced.

Blacks	1, 8 - diaminonapthalene
	o - phenylenediamine
	p - phenylenediamine
	m - toluenediamine
	p - toluenediamine
Browns	o - anisidine
	N, N - dimethyl-p-phenylenediamine
	4 - nitro-O-phenylenediamine
	m - phenylenediamine
	p - phenylenediamine
	p - tolylenediamine
Reds	5 - nitro-m-phenylenediamine
	4 - nitro-o-phenylenediamine
	2 - nitro-p-phenylenediamine
Blue/greys	m - phenylenediamine
	p - toluenediamine

Miscellaneous Aromatic Amines used:

4	- methoxy-m-phenylenediamine
m	- aminophenol
p	- aminophenol
4	- amino-2-hydroxytolylene

4.1.4 Photographic Processes

Phenylenediamines are used extensively in both black-and-white and colour photography, especially the latter, as developing agents. The overall process is illustrated in Fig. 4.1.2 using N,N'-diethyl-p-phenylenediamine as the developing agent.

In this example the amine developer is consumer in the reaction.

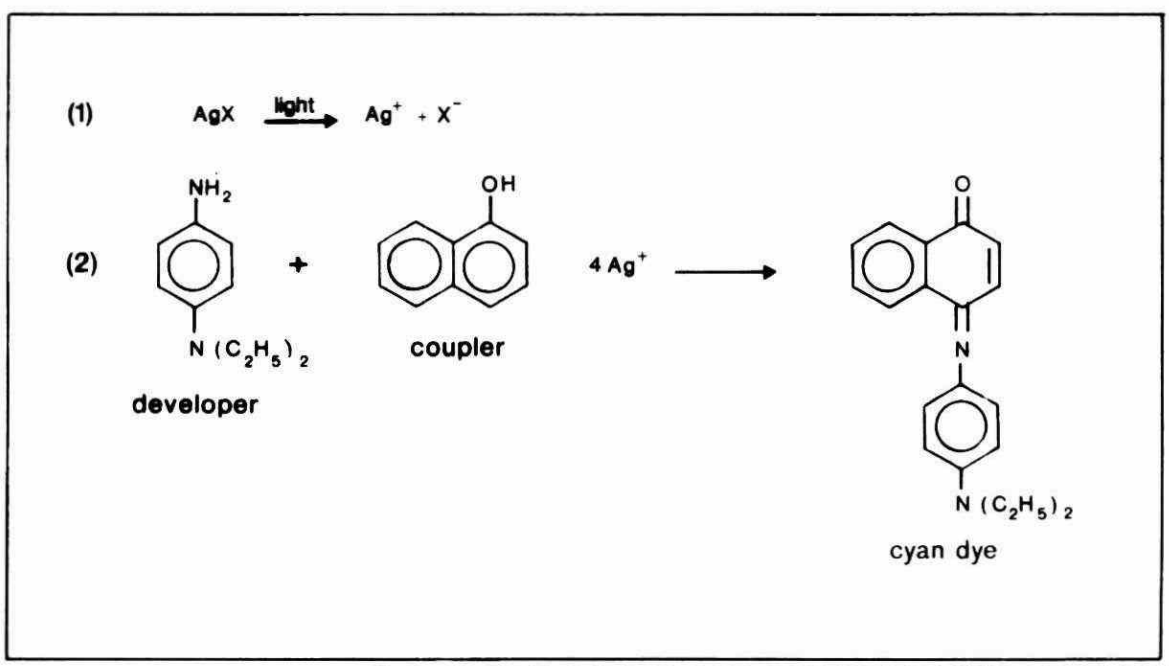


Figure 4.1.2 SIMPLIFIED EXAMPLE OF COLOUR PHOTOGRAPHY PROCESS

The major manufacturer of films and photographic chemicals in Ontario, reported that they import most of their chemicals, including aromatic amines.

The end product, the film, is broadly distributed in quantity. However, because of the nature of the product it is well sealed and isolated from the environment, and does not appear to present a problem.

Numerous small laboratories are involved in the processing of exposed film, and the extent to which pollution control is practiced is uncertain. This industry is of some concern since the processors are numerous and diffuse.

4.1.5 Benzidine Pigments

In Ontario, a number of manufacturers produce pigments. Of these, some are manufacturing benzidine pigments, the most important of which is Pigment Yellow 12.

Consumption of the basic feedstock, 3,3'dichlorobenzidine, is in the order of 200,000 lbs per year producing an estimated one million pounds of mixed products. However, precise figures were not available.

The largest consumers of these products are the paints and printing industries.

Paint is ubiquitous in the human environment. Release into the natural environment will probably occur only when painted materials are landfilled, burned or otherwise disposed of.

A more significant source of pollution may be from the industrial applicators; for example, auto manufacturers.

The problems associated with spray booths and baking ovens are well documented and emissions controls are used extensively. Disposal of paint sludges removed from the paint booths may present an environmental problem.

The printing industry could present some problems in releasing benzidine pigments into the environment. Aerosols observed emanating from the contact plates may contain benzidine pigments. In this connection, no information as

to the ultimate fate of printing sludges or excess inks was uncovered, however, it is believed they are commonly landfilled.

A greater problem may result from the end product, i.e.; the printed page and specialty prints such as wallpapers. These are widely distributed and handled and when discarded they may serve as a dispersion agent into the environment.

A common form of disposal of paper is burning in municipal waste incinerators. Information dealing with the thermal decomposition of pigments under these conditions is not generally available.

4.1.6 Epoxy Coatings and Plastics

Various aromatic amines are used as hardeners in expoxy resins and for various applications in plastics manufacture. Epoxy materials have gained great acceptance because of their ease of application and high degree of chemical resistance. For all intents and purposes epoxy coatings can be considered inert.

In industrial applications, a solution of resin and hardener is mixed and the resultant is applied. With time, the reaction goes to completion, yielding a stable inert material. The same principle is applied in consumer products.

For industrial applications, the hardener can be an aromatic amine such as phenylenediamine or methylenedianiline. Due to the toxicity of these materials, they have been replaced by alkyl polyamines in consumer products.

Fig. 4.1.3 illustrates the general reaction as utilized by both industrial and consumer users. Clearly, the reaction will vary in accordance with the specific reagents utilized.

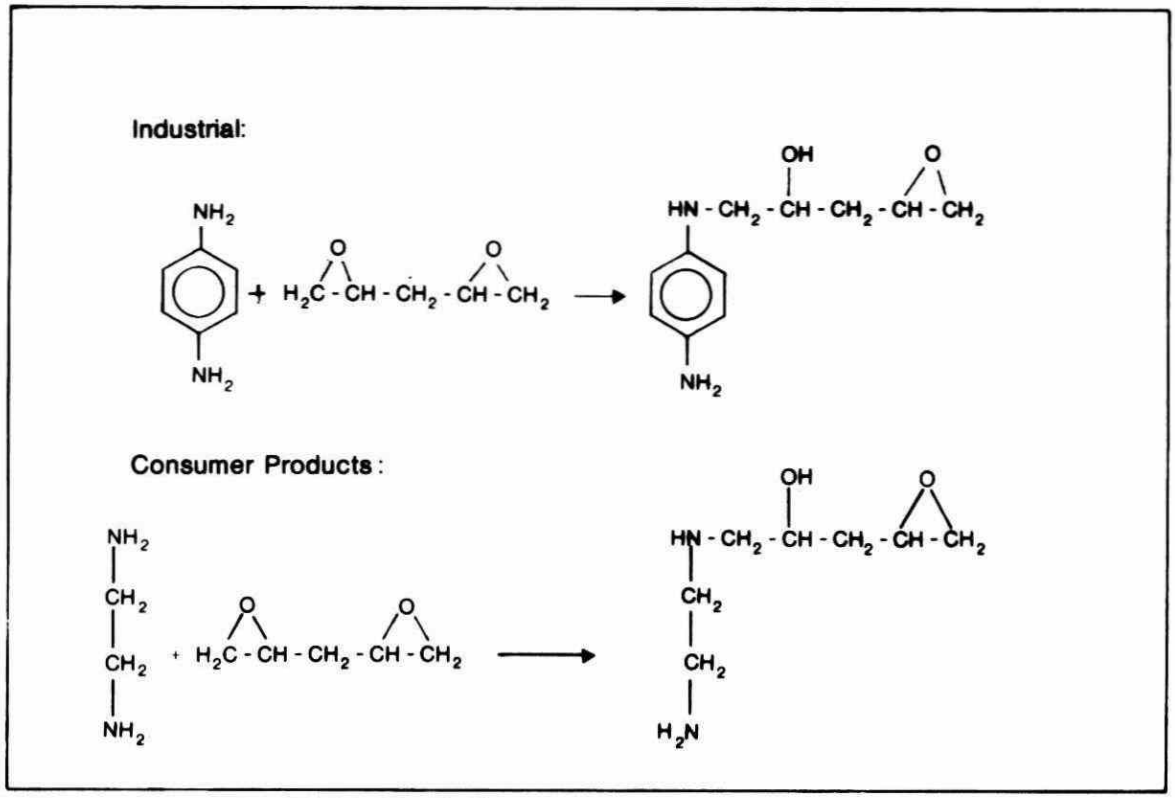


Figure 4.1.3 ILLUSTRATIVE EXAMPLES OF "EPOXY" REACTION

Epoxy coatings in the industrial sector are normally applied by specialist tradesmen. Since the quantities used are generally small, the potential for an environmental release of significance is considered small. Additionally, it seems obvious that the greatest impact of cured resin being released into the environment would be from its lack of degradation rather than the converse.

4.1.7 Petroleum Product Antioxidants

Antioxidants are added to gasoline and oils to prevent their rapid degradation during use and storage. In petroleum products the most commonly used aromatic amines are N,N'-dialkyl-p-phenylenediamines.

The addition of antioxidants to gasoline is a fully enclosed process, normally occurring in the refinery. It is believed normal emission controls are applicable to this process.

It is unlikely that significant quantities of antioxidants are discharged through the process of transfer operations, ie: refinery to consumer's auto. However, it is possible that they are discharged from the exhaust through incomplete combustion in poorly tuned engines.

The greatest potential for emissions lies in the distribution of waste oils. These materials are commonly used for such purposes as road oiling, and as such could be a direct source for emission of aromatic amines into the environment.

4.1.8 Agricultural Chemicals

Aromatic amines are used as precursors in some pesticides, and consequently constitute an integral part of their molecular structure.

In Ontario, there is no primary manufacturing of pesticides. The industry is limited to the importation of the active ingredients followed by blending them with an appropriate carrier. Consequently, the emissions normally associated with primary pesticide manufacture are absent.

A problem may exist with the environmental application of pesticides. In some cases, their degradation may lead to the release of free aromatic amines.

4.1.9 Pharmaceutical Industry

There is no manufacturing of primary pharmaceuticals in Ontario, consequently, none of the emissions normally associated with this process exist.

The industry is limited to importation of the active ingredients and blending them with an appropriate carrier.

In consideration of the cost of imported pharmaceuticals, the processors make efforts to ensure maximum utilization of the drugs. Consequently, discharge of significant quantities of active pharmaceuticals seems unlikely.

4.1.10 Isocyanate Production

In the U.S.A., considerable quantities of aromatic diamines are used in the production of isocyanates. These isocyanates are the major precursors for polymer foam "rubbers". In Ontario, there is only one producer of isocyanates, Allied Chemical in Sarnia. However, this plant is apparently slated for shutdown in the near future.

4.2 AZO DYES

4.2.1 Introduction

No dyestuffs are manufactured in Canada. Statistics Canada reports that in 1976, some ten million pounds of dyestuffs were imported into Canada, mainly from the U.S.A. and Europe. The ten most important colour applications classes for Canada as a whole are tabulated in Table 4.2.1. This table, which is presented for comparison purposes only, does not parallel usage in Ontario.

Information detailing the usage of dyestuffs in Ontario is not generally available in published form. Accordingly, the four leading distributors of dyestuffs in Canada were contacted to provide us with information.

Most of the companies selling dyestuffs in Canada are organized into divisional sections. Each division is essentially an independently functioning unit selling the company's products to a specific industry i.e. textiles, paper and others. This is significant in that each division maintains individual sales records, without detailed knowledge of the activities of the others.

A dyestuff is not usually sold as a pure dye. More commonly it is sold as a formulation containing in addition to the dyestuff, various surfactants, wetting agents and other additives. Each formulation is then sold as a separate product with a specific name designation. This complicates the procedure of determining the quantity of any given dye sold. The sales company will normally keep records of the product designation but not correlate statistics for the formulation or dyestuff itself. Additionally, any given formulation may be sold to different industries under different names.

As explained in an earlier section of this report, the classification of dyestuffs by molecular structure is limited to the manufacturers and a few miscellaneous agencies. The majority of individuals handling or using dyes, classify them by application characteristics, regardless of chemical structure. This is also true for the distributors who maintain sales records in various forms of convenience, none of which is based on molecular structure.

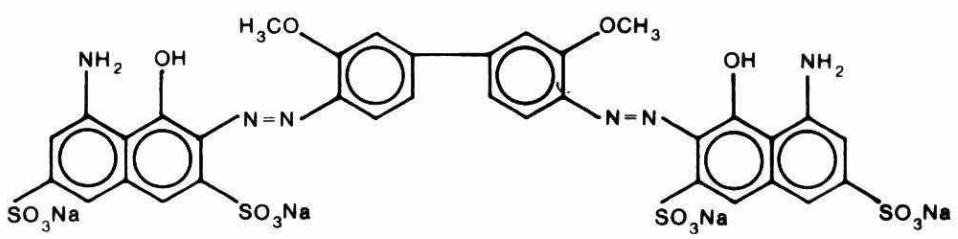
In addition to the foregoing the dyestuffs distribution industry in Canada is very competitive. The competitive position of a company can be seriously affected by a competitor's learning of their sales statistics. Understandably, therefore, some companies, while being most co-operative, were guarded in the information they provided.

These difficulties not withstanding sufficient information was obtained to provide a general overview of the use of dyestuffs in Ontario.

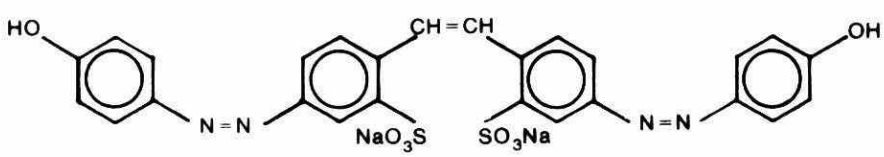
In Ontario, some one hundred dyes are used in quantity. The average usage, representing the majority of dyestuffs is 1200 kg, with the maximum of 25 000 kg per year.

The important dye classes in descending order of importance are: disperse dyes, acid dyes, basic dyes, direct dyes.

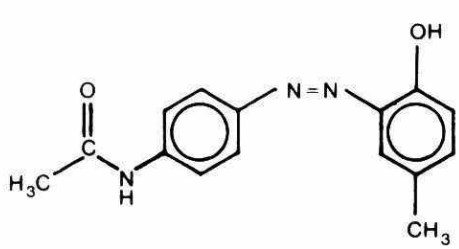
Of the one hundred important dyes, only a few are azo dyes, and a selection of these is listed in Table 4.2.2. The three leading azo dyes are: direct blue 218, disperse yellow 3, direct yellow 4; their structures are illustrated in Figure 4.2.1.



Direct Blue 218



Direct Yellow 4



Disperse Yellow 3

Figure 4.2.1 REPRESENTATIVE EXAMPLES OF AZO DYES USED IN ONTARIO

TABLE 4.2.1

MOST IMPORTANT DYE GROUPS IMPORTED INTO CANADA (1976)

	Dye Groups	Quantity in Pounds
1.	Basic Violets	845 305
2.	Direct Yellows	816 942
3.	Disperse Blues	632 725
4.	Acid Reds	552 055
5.	Acid Yellows	435 869
6.	Basic Blues	432 273
7.	Disperse Yellows	364 817
8.	Acid Blues	351 680
9.	Disperse Reds	326 645
10.	Acid Blacks	249 748

TABLE 4.2.2

MOST IMPORTANT AZO DYES USED IN ONTARIO

(Listed by Application Class)

Basic Red 50	Disperse Red 1*
Basic Blue 78	Disperse Yellow 3
Basic Red 29	Disperse Orange 5
Basic Red 18	Disperse Blue 139
Direct Black 33	Acid Red 337
Direct Blue 218	Acid Orange 107
Direct Yellow 4	Acid Yellow 151
	Acid Red 42

* Numbers identify a specific dye in any given group.

TABLE 4.2.3

APPROXIMATE DISTRIBUTION OF DYESTUFFS IN ONTARIO

Pulp and Paper	-	50%
Textiles	-	40%
Misc.	-	10%

The distribution of dyestuffs in Ontario is between the paper industry, textiles and miscellaneous uses, as presented in Table 4.2.3.

4.2.2 Paper Industry

The paper industry absorbs some 50% of all the dyestuffs used in Ontario. The manufacture of paper can be divided into two phases: pulping the wood and milling the final paper product. The raw materials generally used in the pulping phase are wood, cotton or linen rags, straw, hemp, esparto, flax and jute or waste paper. These materials are reduced to fibres which are subsequently refined, sometimes bleached, and dried.

If a coloured paper is desired, dyes are added, most commonly during the pulping stages. A limited amount of paper is dyed by dip dyeing sheets of finished paper or by spray dyeing at the collanders, the latter two processes occurring in the paper mill.

The paper fibre industries produce two main waste streams, namely pulp mill and paper mill wastes.

The pulp mill wastes contain a broad spectrum of materials including dyes. Current treatment processes may not prevent release of these dyes into the environment.

Similarly, the paper mill wastes contain dyes as only one of the many wastes in their effluent waters.

The final product, the paper, may also represent a route for environmental contamination. The normal form of disposal of discarded paper is to either landfill or incineration.

4.2.3 Textile Industry

The textile industry absorbs some 40% of the dyestuff used in Ontario. In this province, the emphasis is on processing synthetic fibres, with the treating of natural fibres assuming a minor role.

These synthetic fibres are used in the manufacture of carpeting, upholstery fabrics, tire bodies and personal apparel.

The aqueous discharges from textile mills contain dyestuffs. Textile wastes are generally coloured, highly alkaline, high in BOD and suspended solids, and high in temperature. Wastes from synthetic-fibre manufacture resemble chemical manufacturing wastes and their treatment depends on the chemical process employed in the fibre manufacture.

The textile industry has long been a major water user and there has been limited success in developing low-cost treatment methods, which lessen the pollution loads it discharges to the environment.

4.2.4 Home Dyes

Some dyestuffs are commonly sold in drug and grocery stores for use by consumers in home dyeing.

These dyes are designed for use on all common fabrics and consequently, contain a mixture of direct, acid and basic dyes. The direct dye component is always present to facilitate dyeing of cotton fabrics.

Since most direct dyes are benzidine based, and free benzidine is often found in the dye as a residue from the manufacturing process, these dyes may present a significant hazard to the unwary consumer.

Attempts to confirm data on the formulations of these products were not successful. Consequently, precise data on the expected residual levels of free benzidine and other aromatic amines is not available.

These dyes may present an environmental hazard, in that during normal use they are not entirely depleted. In practice, the hobbyist makes the solution and dyes articles in a suitable container. After use, the excess dye solution is flushed into the sewer.

Since some two million pounds of dyestuffs are sold to hobbyists in Canada every year, they may constitute a significant environmental loading.

4.2.5 Miscellaneous

The miscellaneous category accounts for only approximately 10% of total dye consumption and the applications enter into every aspect of life.

Consequently, the environmental emissions from this category may be a small hazard when compared to that presented by paper and textiles.

Methods of disposal of dyed discarded consumer products should be similar to those for paper and textile products, therefore their individual environmental impacts would be indistinguishable, although additive.

ENVIRONMENTAL CHEMISTRY 5

5.1 SYNOPSIS

In this section, the reaction of aromatic amines and azo dyes with respect to a number of agents has been examined.

Both classes of compounds were demonstrated to react with both chlorine and ozone. However, the evidence suggests that the reactions were limited to simple ring substitutions in each case and not the environmentally desirable gross degradations. Consequently, in the case of azo dyes, the manifest effect was decolourization. While this may satisfy visual aesthetics, it is of dubious value in reducing the overall effect on the environment.

When the compounds were subjected to photolysis, the aromatic amines showed some fragmentation under high intensity radiation while azo dyes showed virtually no reaction.

The fragments identified after photolysis of aromatic amines are for the most part resonance stabilized compounds which would be expected to persist for a period of time before autohomolysis.

When exposed to activated sludge, aromatic amines for the most part showed a high degree of resistance to biodegradation. Azo dyes distinctly demonstrated a high degree of toxicity to the micro-organisms and did not demonstrate any disposition for biodegradability. This was observed even after extended attempts to condition the sludge.

In the case of azo dyes, environmental stability would be expected. The commercial market demands a high standard of product performance in terms of durability. Consequently, dyes are designed specifically to be resistant to natural degradative agents, both chemical and biological.

5.2 BIODEGRADATION

5.2.1 Background and Theory

Biodegradation can be loosely defined as the process in which the integral structure of a molecule is changed through microbial action. These changes range from minor structural alterations to major attack resulting in the total disintegration of the molecule. Three distinct levels of biodegradation are defined:

(a) Primary degradation. This is biological action to the minimum extent necessary to change the identity of the molecule.

(b) Acceptable degradation. This is biological action to the minimum extent necessary to remove some undesirable characteristic of the compound, such as foaminess or toxicity.

(c) Ultimate degradation. This is total reduction of the molecule to carbon dioxide, water and inorganic components.

Microorganisms are able to degrade molecules of many types, particularly organic materials. Many synthetic molecules are biodegradable if they show structural similarities to naturally derived compounds.

In order for a biodegradable compound to be subjected to substantial microbial attack, it must satisfy two constraints:

(a) It must exist in concentrations, in relation to other biodegradable compounds, sufficient to provide an "attractive" source of nutrition to microbes. Substrates in trace quantities are subject to biodegradation only if they are more easily degradable or are more "attractive" than those in higher concentrations.

(b) The biomass must be acclimatized to the particular substrate in question. Discharge of a material to unacclimatized biomass may result in the death of a significant proportion of the microorganisms, with a resultant general decline in effluent quality.

A microorganism may not be able to attack an entirely new compound on first exposure. In fact, the compound may be acutely toxic to the biomass. However, if the new compound is introduced slowly in low concentration over an extended period of time, it is possible that the microbe population may adapt and eventually begin to degrade the substrate. This adaptation process is termed acclimatization.

It should be emphasized that while acclimatization is a common phenomenon, it is an error to think that given enough time any compound can be biodegraded. Some compounds are simply not biodegradable.

5.2.2 Activated Sludge Treatment

Activated sludge is the most common process in use today for the treatment of oxygenated municipal wastewaters. The process requires the blending of the waste with a large mass of acclimatized microorganisms, which through metabolic processes, effect reduction of the substrates.

A large proportion of aromatic amines and azo dyes discharged into the environment may be routed through municipal sewers to activated sludge treatment plants and this being the case, activated sludge may play a role in their degradation.

Under experimental conditions, the rate of biodegradation of a substrate can be estimated by subjecting it to the Warburg respirometer test. This test can be related, by extrapolation, to environmental conditions.

In the test, the substrate is fed to an acclimatized population of microorganisms and the subsequent total uptake of oxygen is measured as a function of time. The rate of uptake of oxygen is related to the rate of degradation of the substrate.

For control purposes, a separate colony of bacteria is maintained which is not fed the substrate. During the period of the experiment, the oxygen uptake by the control group is also measured.

When the two curves are compared, it can be assumed that if the substrate curve is above the control, biodegradation is occurring. If the substrate curve lies below the control, it can be considered toxic or inhibitory of microbial action.

5.2.3 Biodegradation of Aromatic Amines

Aromatic amines have been shown to have varied responses to biological degradation in activated sludge.

In one experiment, aniline was toxic to activated sludge. After a conditioning period of twenty days, the sludge acclimatized and began to degrade aniline. As can be seen from Figure 5.2.1 when acclimatized microbes were fed aniline the major portion of oxygen uptake was recorded in the first sixty hours.(1) However, when a similar acclimatized sludge was treated with the ortho and para phenylenediamines, they showed a significant resistance to biodegradation. At the termination of the experiment, after 190 hours, the biomass had utilized only approximately one half the quantity of oxygen measured in relation to aniline under similar conditions. This suggests that these substrates are poorly degradable relative to aniline.

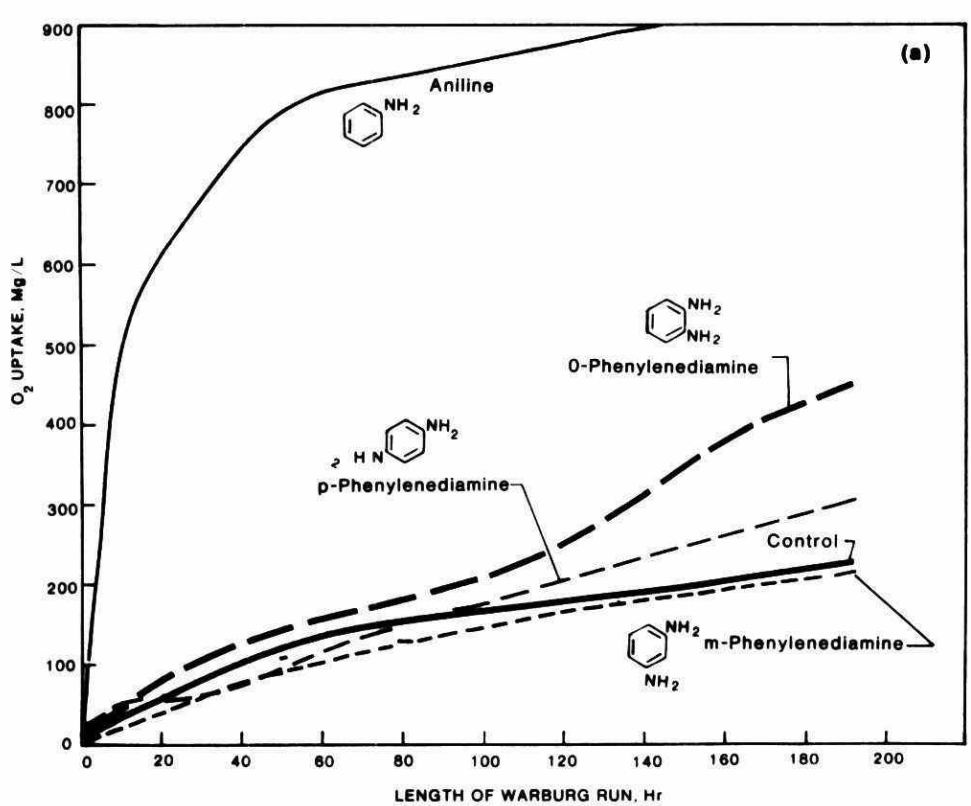


Figure 5.2.1 OXIDATION OF PHENYLENEDIAMINES BY ANILINE-ACCLIMATED ACTIVATED SLUDGE

The curve for meta-phenylenediamine is seen to be below the control curve. This suggests that under these circumstances, it is toxic and not biodegradable.

The oxygen utilization curve for alpha-napthylamine is presented in 5.2.2. Here, it can be seen that this substrate has a much lower rate of oxygen utilization than aniline. In fact, another study has suggested that alpha-napthylamine is distinctly toxic.(2)

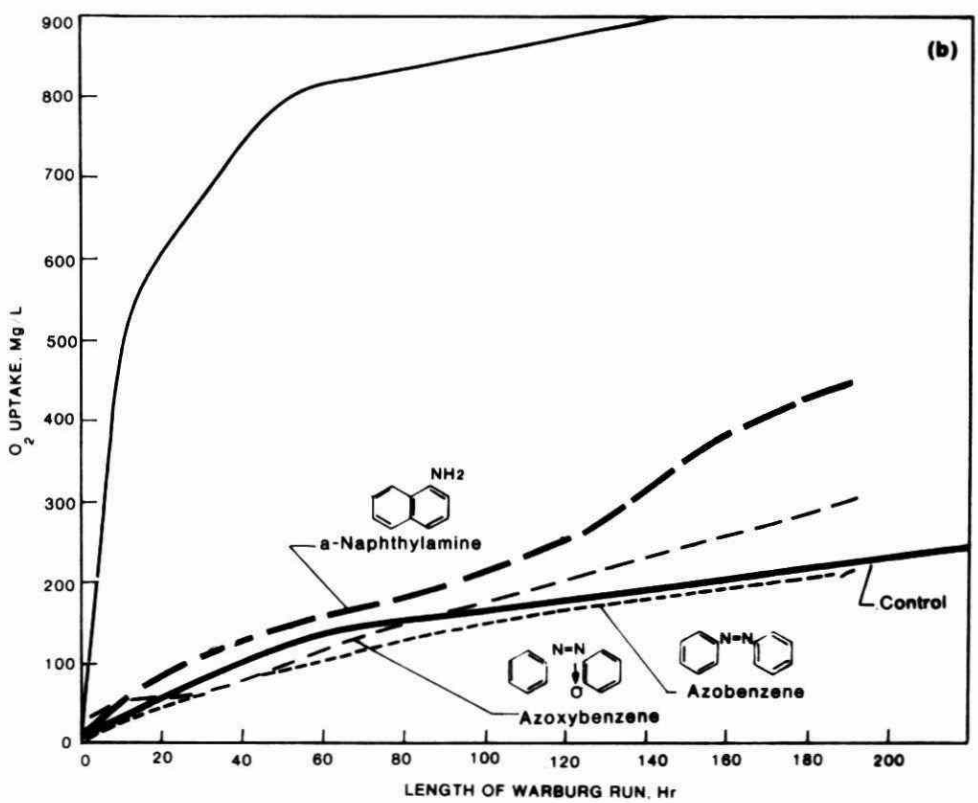


Figure 5.2.2 OXIDATION OF SOME AZO COMPOUNDS AND NAPHTHYLAMINE BY ANILINE ACCLIMATED ACTIVATED SLUDGE

The compounds benzidine and beta-napthylamine were investigated and shown to be toxic to activated sludge.(3) This toxicity persisted even after attempts were made to acclimatize the sludge.

5.2.4 Biodegradation of Azo Dyes

When the azo dyes were investigated for biodegradability, it was found that on the whole they are toxic to activated sludge and in general not amenable to aerobic biological degradation.

In Figure 5.2.2, the oxygen uptake curves for the two simplest aromatic azo compounds are illustrated.(4) Since they are close to the control curve, it can be implied that they are poor candidates for biodegradation.

In a similar study evaluating the biodegradability of coloured textile wastewaters, it was confirmed that dye-stuffs in general are not biodegradable.(5) The figure presented in Fig. 5.2.3 illustrates that a mixed textile wastewater showed rapid degradation of organics for the first few days, after which a steady TOC value was obtained. This steady value was related to non-biodegradable dyestuff, while the degraded material was identified as miscellaneous organic additives.

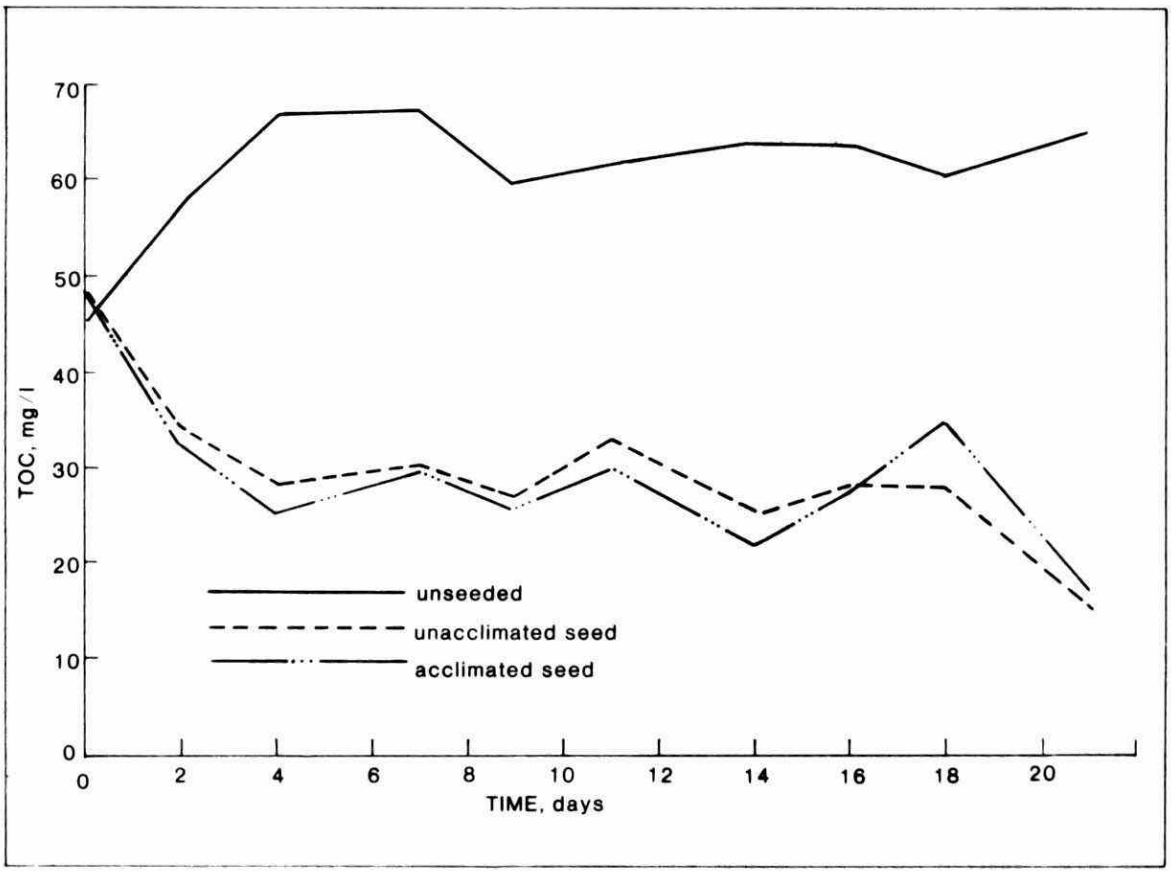


Figure 5.2.3 DYEING WASTEWATER BIODEGRADATION

From these data, it appears that the dyestuffs are not readily biodegradable, and this should not be considered as a detoxification route.(6)

5.2.5 Biodegradation in the Natural Environment

The evidence presented in the previous sections suggests that aromatic amines and azo dyes will resist biodegradation in the natural environment.

5.3 CHLORINATION

5.3.1 Background and Theory

Chlorination is extensively practiced in wastewater treatment to disinfect effluent prior to discharge. This is particularly the case where the receiving water may be used either for recreational purposes or as a source of potable water.

It has been demonstrated that chlorination in municipal treatment plants will increase the toxicity of wastewaters to aquatic life.(7) This increase in toxicity can be linked to the chlorination products of dissolved pollutants.

Two major reactions may occur simultaneously when chlorine is added to water; hydrolysis and ionization. The hydrolysis of chlorine is complete within a few seconds at ordinary temperatures, and the ionization of hypochlorous acid is an instantaneous reversible reaction.(8) These processes are illustrated in Figure 5.3.1. The specific reactions and efficiency of the hydrolysis processes are affected by the temperature, the pH, the buffering capacity of the waters and the specific chlorinating agent applied.

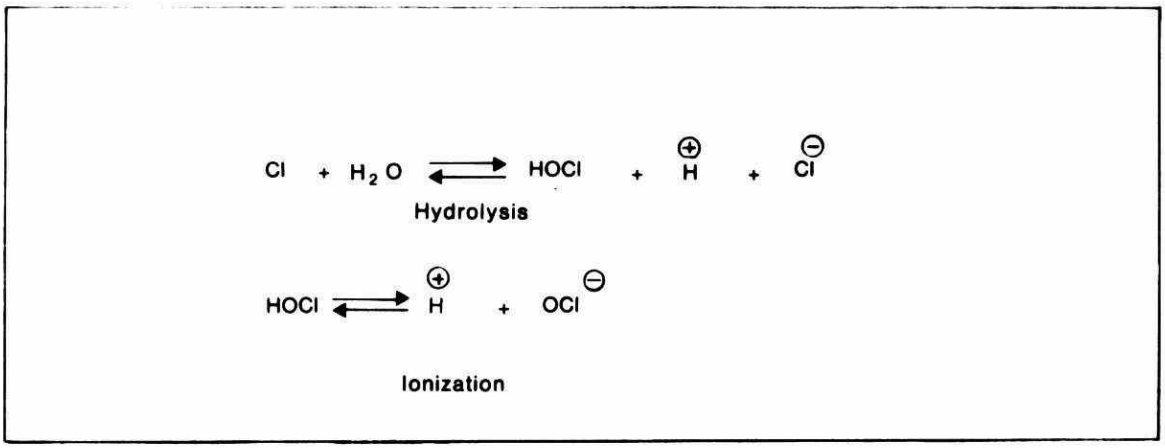


Figure 5.3.1 REACTION OF CHLORINE WITH WATER

Regardless of the type of reaction, gaseous chlorine results in the formation of hypochlorous acid and hypochlorite ions in equilibrium in water. The reactive species is considered to be the hypochlorite ion.

5.3.2 Chlorination of Aromatic Amines

The amino function in an aromatic ring is a powerful ortho/para director with activation. Simple aromatic amines are highly reactive when subjected to electrophilic attack, and under these conditions substitution tends to occur at every available ortho and para position, with some substitution at meta.

Therefore when aniline is exposed to excess chlorine in an aqueous environment, all the products illustrated in Figure 5.3.2 are observed.(9)

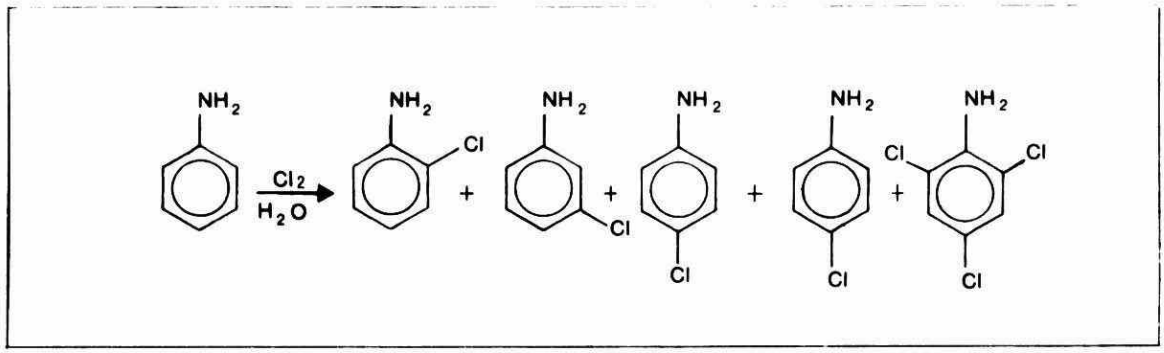


Figure 5.3.2 EXHAUSTIVE CHLORINATION OF ANILINE

Under environmental conditions, it can be predicted that kinetic considerations would probably restrict the products to the monochloro derivatives.

Amines are also subject to N-alkylation. If an amine is reacted with an alkylhalide, a smooth reaction yielding the N-alkyl derivative occurs. In the presence of excess alkylating agent, the reaction proceeds until a tertiary amine is obtained. This reaction, illustrated in Figure 5.3.3 utilizing aniline and chloromethane, is note worthy since various alkylhalides have been detected in drinking water.(10)

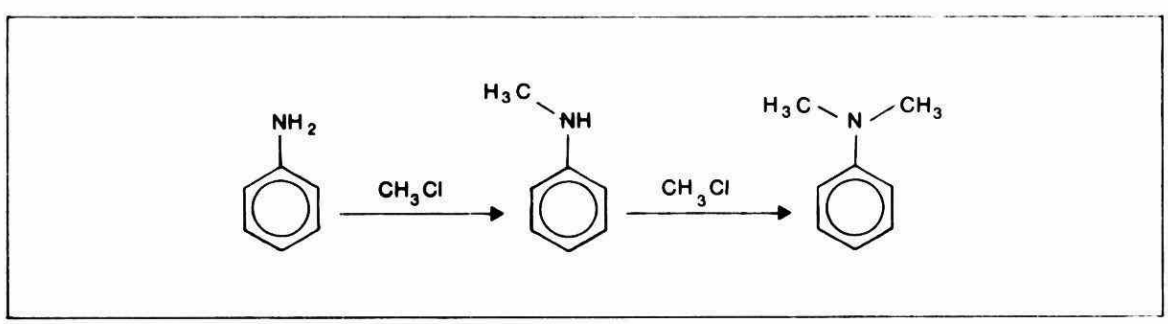


Figure 5.3.3 REACTION OF ANILINE WITH ALKYL CHLORIDES

When aniline, dimethylaniline and benzidine were subjected to chlorination under conditions simulating municipal treatment, a broad range of products was identified.(11)

For all three amines, reaction was rapid and essentially stabilized after twenty minutes. It was observed that the rate of chlorination was a function of chlorine concentration, and these data are presented graphically in Figure 5.3.4.

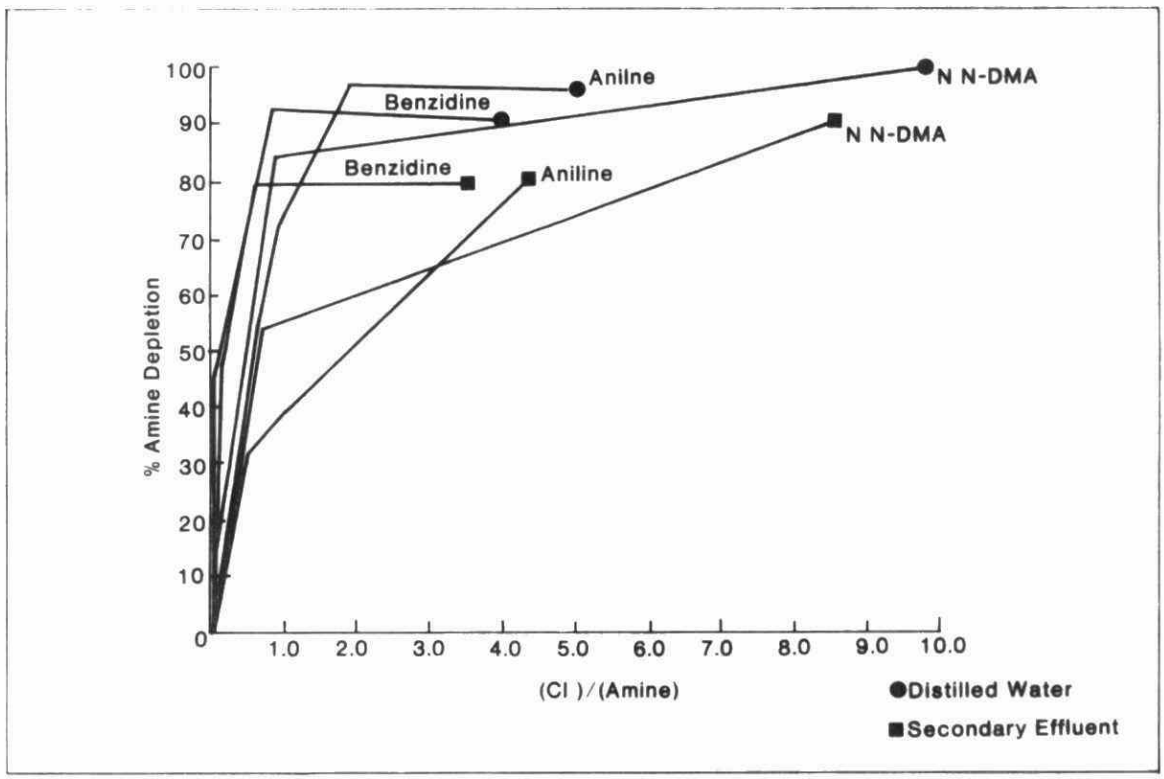


Figure 5.3.4 AMINE DEPLETION AS A FUNCTION OF THE CHLORINE TO AMINE MOLAR RATIO

The primary products identified for aniline under these conditions are illustrated in Figure 5.3.5. These products were determined to account for some thirty percent of the aniline depletion, with seventy percent being unaccounted for. Similar results were observed for dimethylaniline.

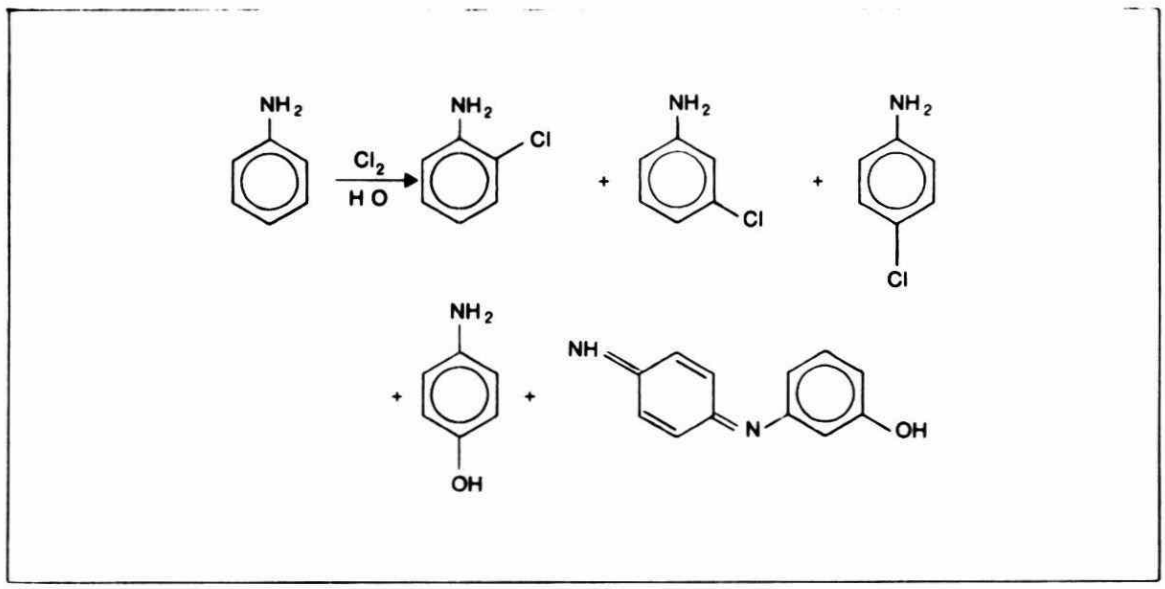


Figure 5.3.5 CHLORINATION OF ANILINE IN WASTEWATER

No evidence for N-chlorination or ring cleavage was observed in either aniline or dimethylaniline, an observation consistent with that expected from kinetic considerations.

Benzidine displayed a unique reaction in that the only product observed was an oxidation polymer. The authors suggest that the structure of this polymer is as illustrated in Figure 5.3.6. This reaction was very rapid and occurred in less than two minutes. The polymer accounted for approximately 80% of the benzidine depletion.

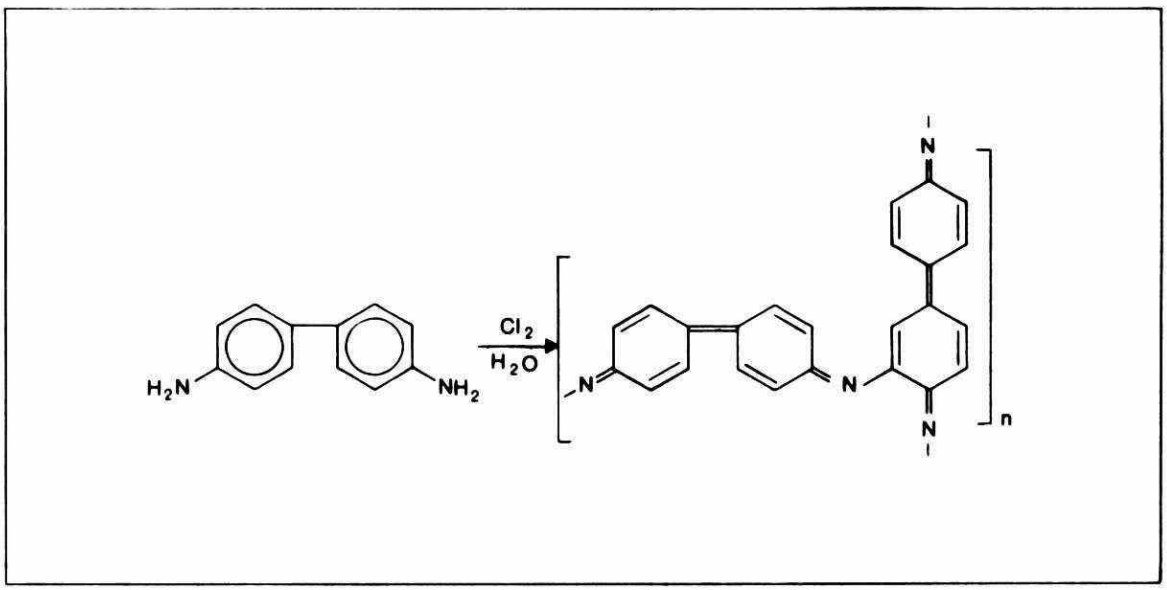


Figure 5.3.6 CHLORINATION OF BENZIDINE IN WASTEWATER

5.3.3 Chlorination of Azo Dyes

During the course of our study, we were unable to uncover any information relating specifically to the chlorination of azo dyes.

However, since most of these dyes are derivatives of the aromatic amines noted in the previous section, it is reasonable to assume they will undergo similar chlorination reactions.

Accordingly, it can be speculated that when an azo dye is subjected to aqueous chlorine, the initial reaction will be ring chlorination. Analogously, as illustrated in Figure 5.3.7, when azo benzene was treated with bromine, the di-para-bromo derivative was obtained.(12) It would be consistent to suggest that chlorination would yield a corresponding product. This chlorination may be sufficiently disruptive to the dye chromophore to shift the absorption bands from the visible. The net observable result may be decolourization of the dye solution.

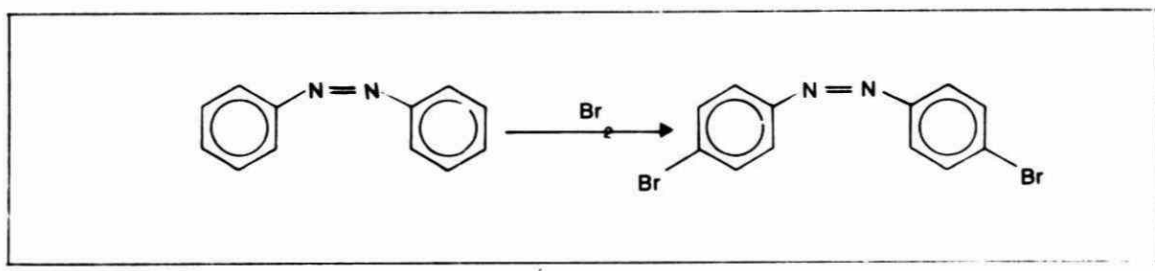


Figure 5.3.7 BROMINATION OF AZOBENZENE

In the case of flourescent tracer dyes, the observed effect of chlorination was a reduction of flourescence intensity.(13) This would seem consistent with the contention that the chromophore will be disrupted, but gross degradation is unlikely to occur.

5.3.4 Chlorination in the Natural Environment

Chlorination in the natural environment is not considered to be a significant depletion route, based on the low concenoentration of free chlorine found in the environment. Simple kinetic considerations imply that the chlorine interactions will be virtually non existent.

5.4 OZONATION

5.4.1 Background and Theory

Ozone is a significant reagent in that it is a natural constituent of the atmosphere and has been implicated in numerous biological and chemical reactions.

It is a highly reactive species that is formed naturally by the action of solar radiation in the stratosphere and by human activity.

The total amount of ozone in the upper atmosphere has been found to vary around the mean concentration of 0.02 ppm. The concentration at sea level near urban centres has been shown to vary, and in some cases is much higher than stratospheric concentration.(14)

Of equal importance is the fact that ozonation has been proposed as an oxidation and disinfection reagent for the removal of organic substances from potable water in Ontario.

Research is presently underway in an attempt to quantify the importance of ozone as an environmental factor. The relative importance of ozone in corrosion of materials, and in the degradation of pollutants in the environment is not clearly understood.

Ozone is a powerful oxidizing agent and is capable of causing oxidative degradation of many organic compounds.(15) It primarily attacks unsaturated organic compounds, particularly olefinic double bonds, and to a lesser extent aromatic compounds.

There are three mechanisms by which ozone is known to react, the predominance of one or other is governed by specific reaction conditions.

The most general mechanism of attack by ozone on a double bond is illustrated in Figure 5.4.1. There it can be seen that the initial reaction product is a primary ozonide. This ozonide decomposes thermally to a carbonyl function and a zwitterion.(16)

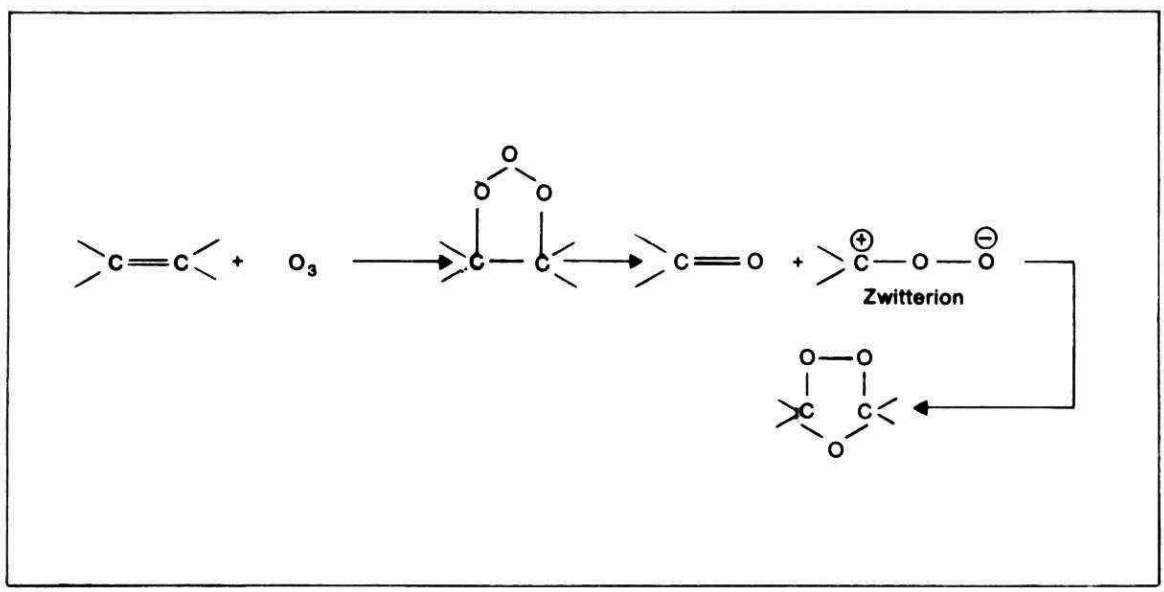


Figure 5.4.1 OZONOLYSIS OF A GENERAL OLEFIN

The zwitterion can react with other available species, but more generally, it recombines to form another ozonide. The reaction kinetics favour recombination over third substrate reaction.

Another mechanism by which ozone is known to react involves a dipolar electrophilic interaction. This is illustrated in Figure 5.4.2 in which a nucleophilic amine reacts with the dipolar ozone to form an activated complex.(17)

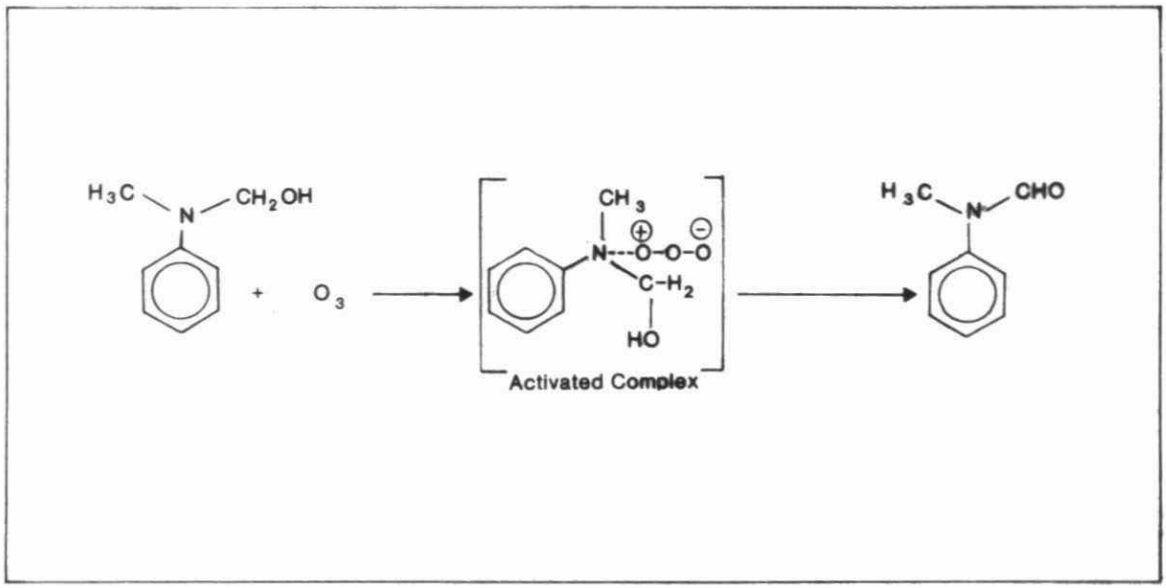


Figure 5.4.2 OZONOLYSIS BY DIPOLAR MECHANISM

A third mechanism involves the creation of a free radical species effected by ozone. This mechanism is similar to that illustrated in Figure 6.2.6 which can be generalized to include all species.

When an aromatic molecule is subjected to intensive ozonolysis under vigourous conditions, the ring is cleaved and drastic degradation occurs. This is illustrated in Figure 5.4.3 in which phenol is used as a specific example.(18) The final product, oxalic acid, is apparently resistant to further degradation.

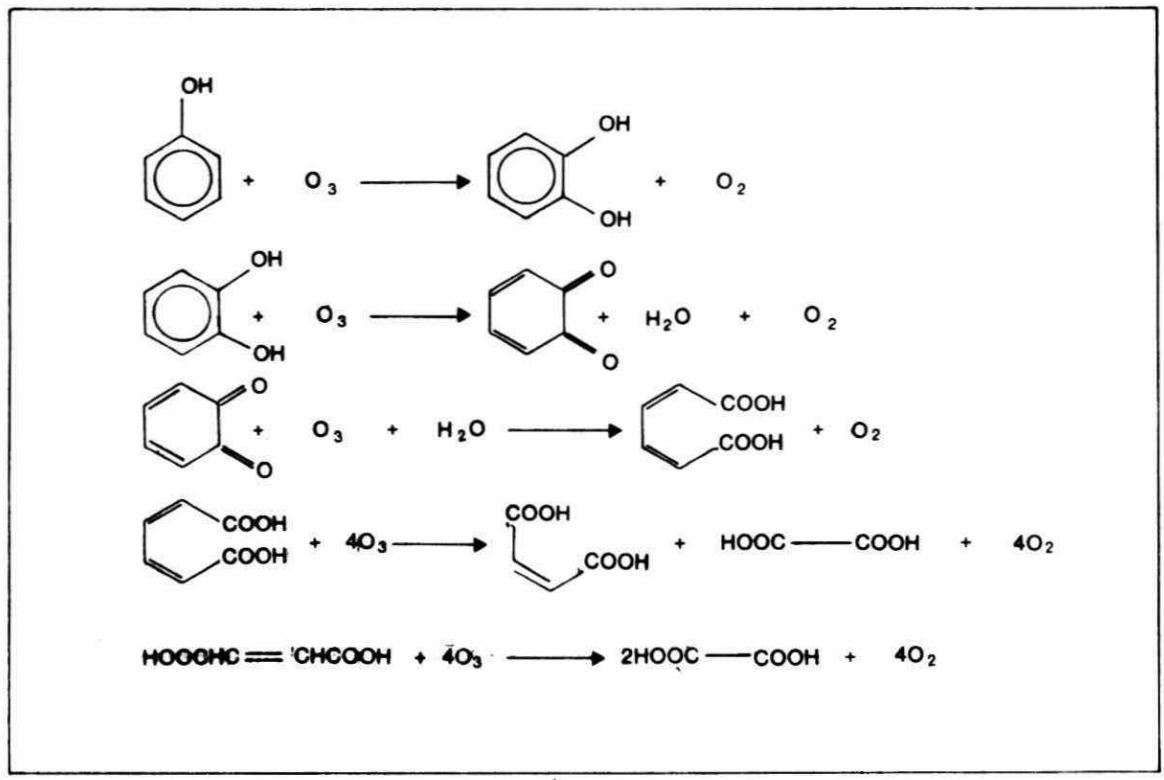


Figure 5.4.3 EXHAUSTIVE OZONOLYSIS OF PHENOL

The illustrated reactions are instructive of the potential of ozone to effect degradation of molecules under laboratory conditions in which ozone concentrations are high. However, when ozone is used as a wastewater disinfecting agent the concentrations and contact times will be considerably less. Therefore extensive oxidation should not be expected, in fact, total degradation is rare.

5.4.2 Ozonation of Aromatic Amines

The degradation of aromatic amines under ozonolysis conditions has not been extensively studied and consequently, there is a shortage of information available.

In one study, the oxidation of N-alkylated aromatic amines was studied. In the reaction of N,N'-dimethylaniline, illustrated in Fig. 5.4.4 the predominant products identi-

fied were: N-methylaniline, N-formylaniline, and an ozonide dimer. Analyses of the relative proportions of the products were equivocal.

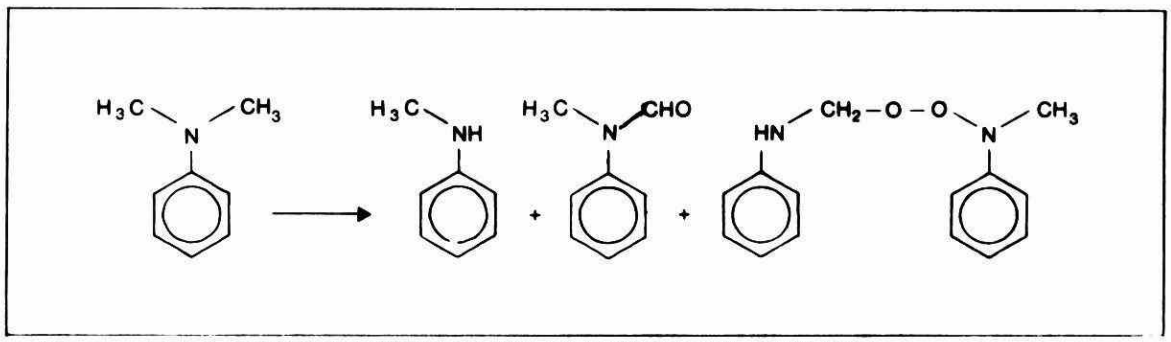


Figure 5.4.4 OZONOLYSIS OF N, N DIMETHYL ANILINE

The authors did not identify any ring oxidation products and were led to suggest that the N functionality is the preferred point of attack. No attempt was made to subject these substrates to exhaustive ozonolysis in order to determine the ultimate degradation route or products.

5.4.3 Ozonation of Azo Dyes

The discovery that dyes fade under the influence of ambient ozone is reported to have been made by accident in 1955. It was noted that on exposure to air, dyes oxidized and produced less deeply colored molecules. This phenomenon became known as "O-fading"(19).

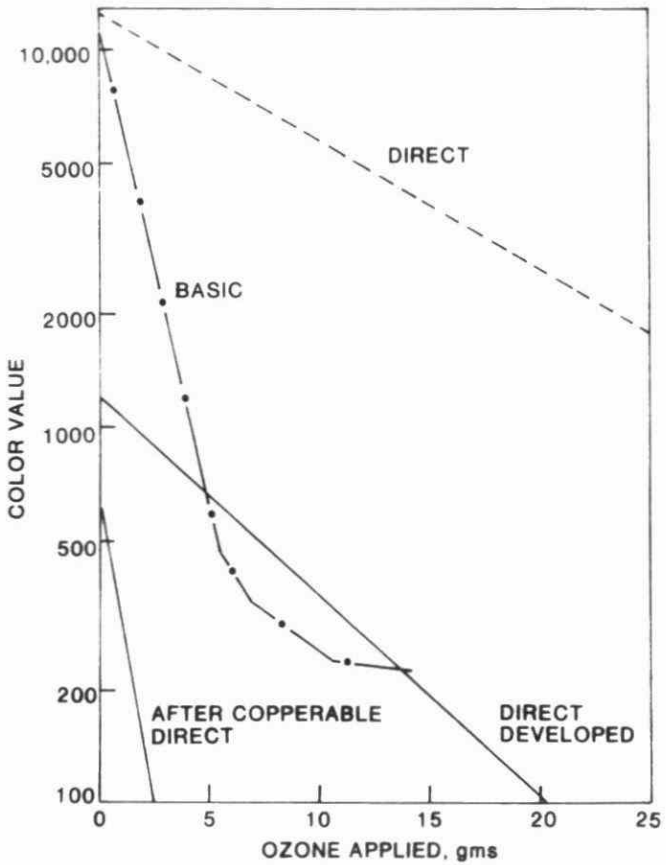
There has been some recent work examining the reaction of dyes to ozone. However, the point of concern in these studies has been examination of the gross effects of ozonolyses. None attempted to identify reaction products or routes. The basis for determination was decolorization.

This is unfortunate in that any reaction causing a disruption in the chromophore is bound to cause colour varia-

tions. Therefore, even though a dyestuff solution may be decolorized, the integral structure may still remain intact.

In a study by Snider(20), the effect of ozone on textile wastewaters was examined. These wastewaters contained mixed organic materials in addition to dyes. It was noted that ozone effectively reduced the coloration and COD of the mixed solution. However, the COD reduction was not related specifically to dyestuff degradation.

In a more comprehensive study, textile dye wastes were subjected to extensive ozonolysis with the objective of quantifying dye application classes relative to their susceptibility to ozone decolorization (21) The results, which are adapted for this report, are illustrated for a group of azo dyes in Figure 5.4.5. They show that the effectiveness of decolorization varied considerably between classes of dyes.



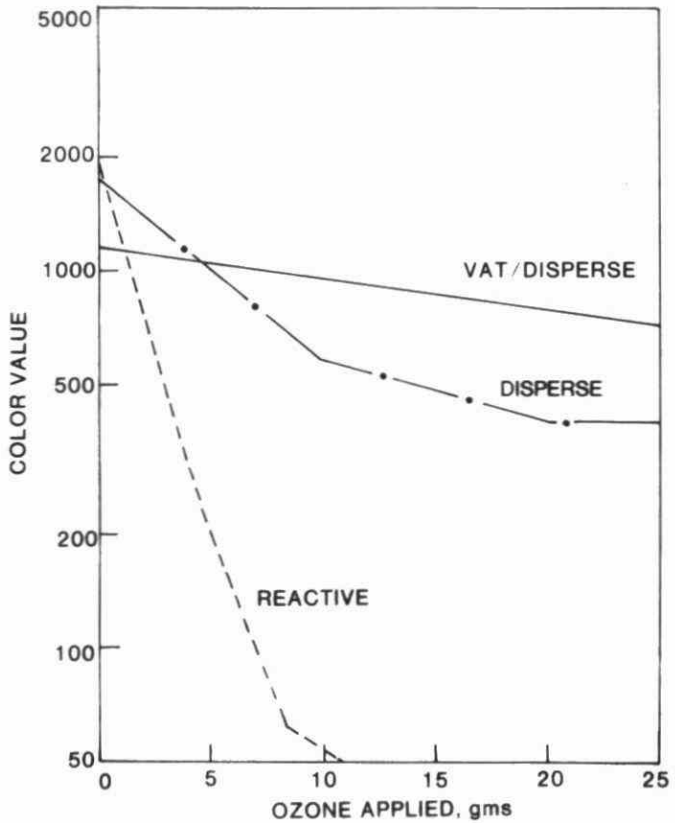


Figure 5.4.5 COMPARISON OF SOME DYEING WASTEWATERS WITH RESPECT TO DECOLORIZATION BY OZONE

Reactive dyes were very effectively decolorized, with a colour reduction of approximately 95%. In comparison however, disperse dyes were poorly decolorized.

It was observed that basic dyestuffs were decolorized to a constant residual level, which could not be lowered even with extensive treatment. This is significant in that it supports the contention that decolorization may occur simply by changing the chromophore. In the case of basic dyestuffs, the disruption served merely to change the colour, but was insufficient to move the absorption curve from the visible.

5.4.4 Ozonation in the Natural Environment

The atmospheric concentration of ozone at sea level is approximately 0.02 ppm.(22) However, this concentration varies depending on the specific recording location, and its proximity to major urban centres.

In consideration of the reported fading of dye stuffs in the atmosphere, it would seem that their reaction with ozone may be a significant degradation pathway.

The rate of absorption of ozone from the atmosphere into natural waters is still under study, but is believed to be site specific due to the variations in atmospheric concentration. However, the overall transfer rate seems low.

Once absorbed, the ozone will react indiscriminately with susceptible organics, resulting in a rapid depletion of ozone. Consequently, if the pollutant loading is high, ozone will have to have a low relative effect. Similarly, it can be expected that the reaction zone is quite shallow and near to the surface.

Until more data is available on the environmental concentrations of aromatic amines and azo dyes, it is difficult to evaluate the impact of ozone on their depletion from the environment.

5.5 PHOTOCHEMISTRY

5.5.1 Background and Theory

Photochemistry deals with a unique type of chemical reaction. It is concerned with an interaction between a light quantum and a molecule with a resultant physical or chemical change.

When light radiation of a particular frequency falls on a molecule, it may or may not be absorbed. In the case of sunlight, which consists of a mixture of frequencies, some frequencies may be absorbed, with the remainder being reflected. One immediately perceived result may be that the compound appears coloured.

Molecular quantum theory contends that every molecule has electrons in defined orbitals or energy levels. These orbitals have a characteristic energy, each of which contributes to the total energy of the molecule. The minimum total energy condition is referred to as the ground state, and is the preferred state for any molecule.

The absorption of light induces an electron to move into a higher energy orbital, where it exists in an unstable state. Consequently, this state is referred to as an excited state.

This increase in energy can occur only through the absorption of specific quantities of energy, or quanta. The amount of energy required to promote an electron to an excited state is characteristic of each molecule, and serves to explain why molecules can be seen to have different colours.

A greatly simplified illustration of this process is presented in Figure 5.5.1, in which an electron is promoted from energy level E_0 to the first excited state E_1. The energy of the electronic transition from V_0 of the ground state to V_0 of the excited state is exactly equal to the energy of the absorbed light, which is given by hv.

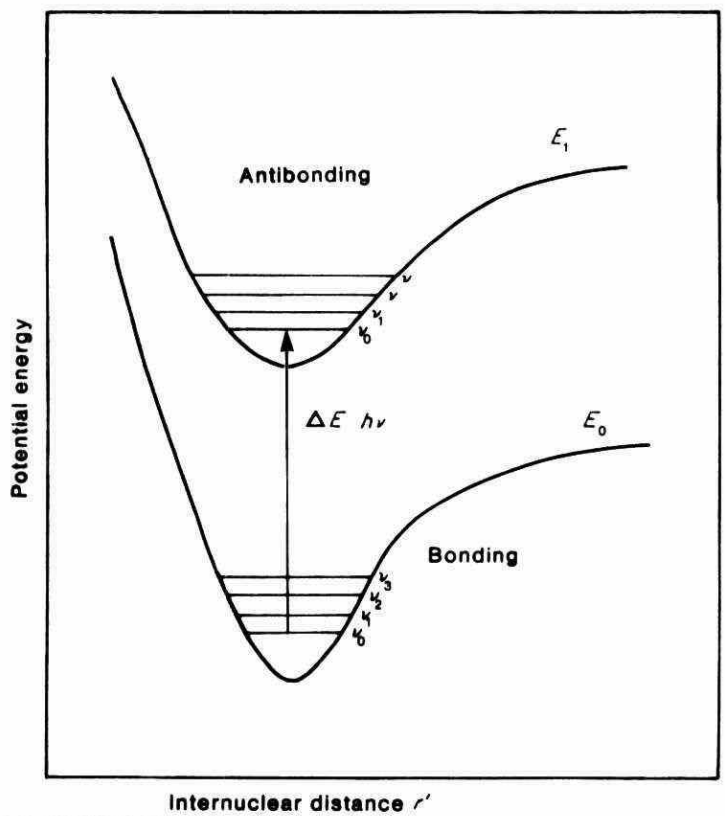


Figure 5.5.1 POTENTIAL ENERGY CURVE FOR AN ELECTRONICALLY EXCITED AND GROUND-STATE DIATOMIC MOLECULE

As noted previously, the excited state is an unstable condition and consequently the molecule moves to revert to the preferred ground state.

The major events that occur following light absorption may be summarized in terms of a "Jablonski diagram". The absorption of light raises the molecule from S_0 to S_2, as shown in Figure 5.5.2.

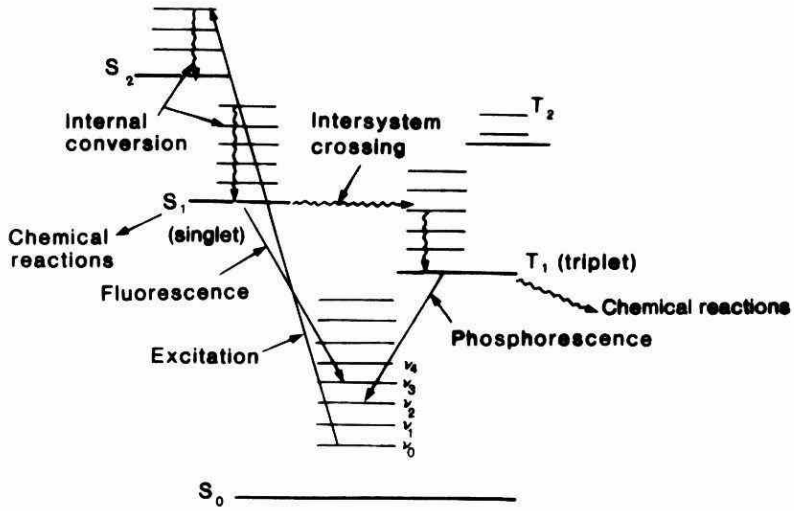


Figure 5.5.2 JABLONSKI ENERGY DIAGRAM

In solution, the excess vibrational energy of S_2, will be rapidly dissipated by radiationless processes thus reducing molecular energy level to S_1. After conversion to S_1, the molecule may lose its energy by four important processes: (a) fluorescence, (b) chemical reaction, (c) return to a highly vibrationally excited ground state (S_1-S_0) and (d) intersystem crossing.

Intersystem crossing (S_1 to T_1) occurs between two excited states of similar energy and is very important in photochemistry, because the triplet state T_1 produced is even longer lived than S_1. The lifetimes of T_1 are limited by: (i) phosphorescence, (ii) chemical reaction and (iii) radiationless decay to S_0.(23)

5.5.2 Photosensitization

Photosensitization involves the process whereby one chemical species absorbs light energy and then transfers this energy to another species. This excited molecule can react by either returning to the ground state or undergoing chemical transformation.

Many dyes are well known sensitizers. This aspect has not been thoroughly investigated in the context of environmental degradation. However, it has been speculated that this particular property of dyestuffs may be a factor in their degradation in the environment.

It has been suggested that dyestuffs may act as sensitizers and create highly reactive singlet oxygen. Singlet oxygen may then react with the dyestuff, yielding an oxidation product. Therefore, the dyestuff is instrumental in its own destruction.

This particular hypothesis has not yet been fully investigated. However, as one example, it is noted that in plants, chlorophyll which is a well known sensitizer, is always found in conjunction with a high concentration of keratins. Keratins are well known singlet oxygen scavengers. This reacting couplet allows chlorophyll to proceed with the essential process of photosynthesis without concomitantly causing the destruction of the plant.

There are published reports of inorganic materials, such as common sand and iron oxides, functioning as photosensitizers instrumental in the decomposition of organic materials. In one report, 87% of a phenol solution was seen to degrade in 72 hours when exposed to light on a common beach sand catalyst.(24) In another paper, Titanium dioxide was noted as a photosensitizer in the decolourization of dyes in paints. In this study, a solution of an azo dye, "Blue FF", showed marked fading when irradiated in the presence of titanium oxide catalyst. This fading was not observed under similar reaction conditions in which the titanium oxide was absent.(25)

5.5.3 Photolysis of Aromatic Amines

The photochemistry of aromatic amines as distinct entities in the environmental context has not been studied.

However, some amines have been photolyzed during kinetic and theoretical studies. These data, while not directly applicable to the environmental context, are nevertheless instructive in gaining an overall perspective.

The primary photodissociative processes of the amines are open to question. Definitive studies have been made only on the simplest amine, methylamine. In this case, and apparently in the other primary aliphatic amines, photodissociation occurs largely by the process, illustrated in Figure 5.5.3, of formation of hydrogen atoms and alkylamine radicals.(26)

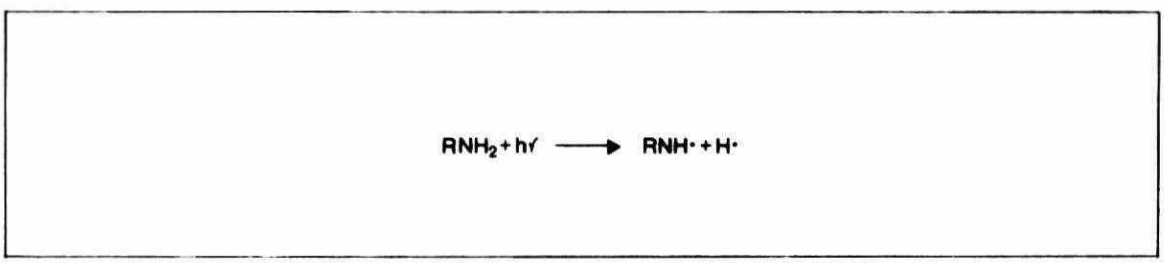


Figure 5.5.3 PHOTOLYSIS OF PRIMARY ALKYLAMINES

In secondary aliphatic amines, dissociation of the nitrogen carbon bond has been suggested, in addition to hydrogen atom formation, as illustrated in Figure 5.5.4.

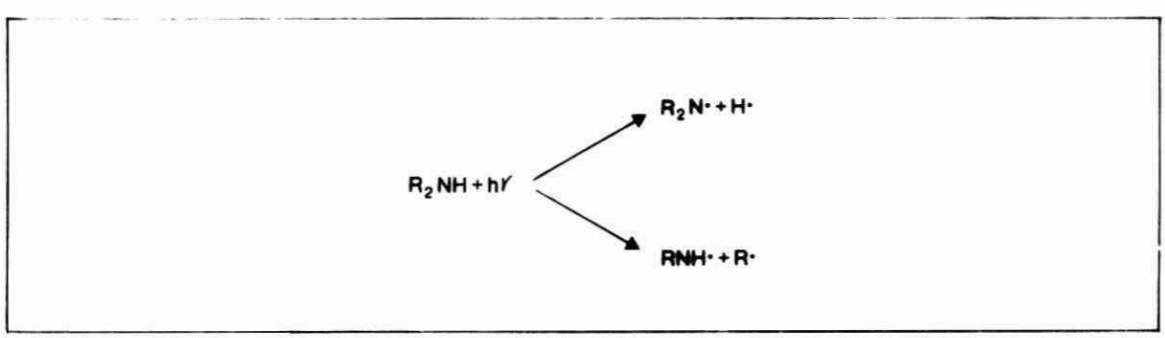


Figure 5.5.4 PHOTOLYSIS OF SECONDARY ALKYLAMINES

Figure 5.5.5 illustrates the photoreactions of tertiary aliphatic amines. The carbon-nitrogen dissociative process predominates, but molecular re-arrangement and down chain carbon-carbon cleavage has been observed.(26)

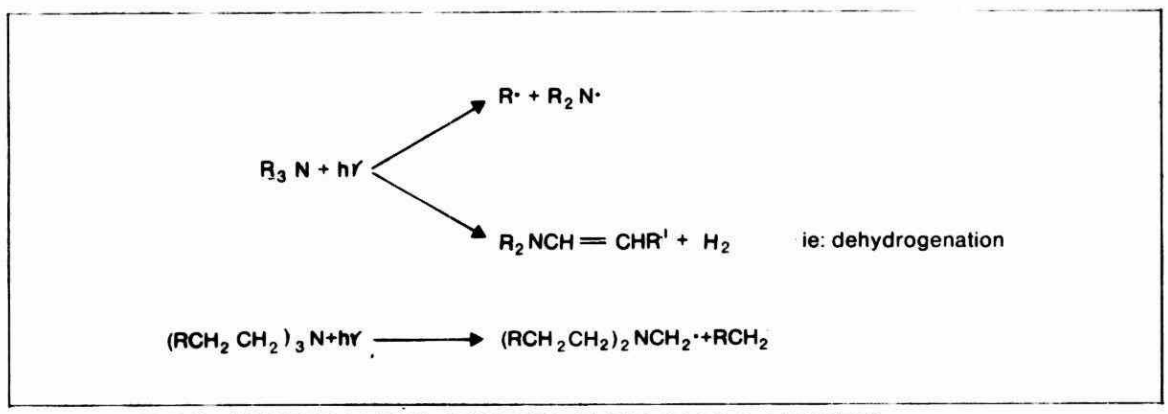


Figure 5.5.5 PHOTOLYSIS OF TERTIARY ALKYLAMINES

The aromatic amines are considerably more stable photochemically than their aliphatic analogs. Fluorescence is a deactivation mechanism very commonly encountered in these systems.

When aniline was photolysed with a full mercury arc, the primary deactivation route was fluorescence. However, at elevated temperatures N-dehydrogenation and deamination occurred.(26) These processes are illustrated in Figure 5.5.6.

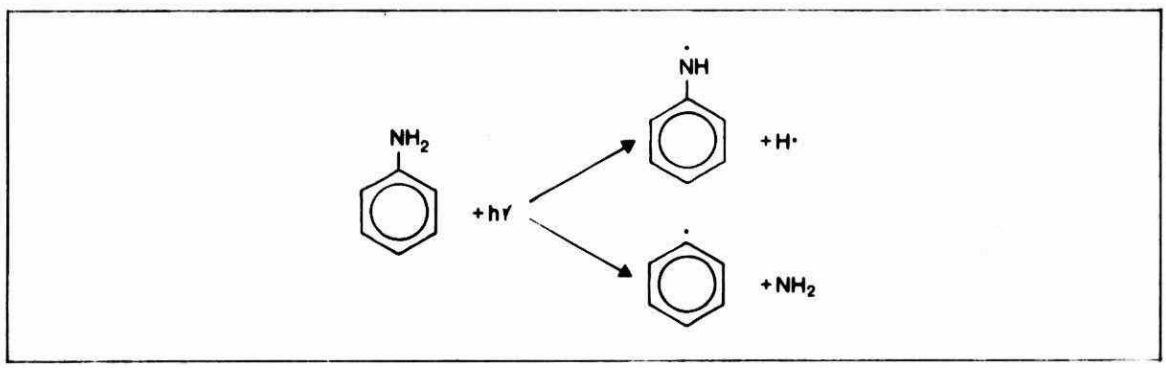


Figure 5.5.6 PHOTOLYSIS OF ANILINE

When diphenylamine and triphenylamine were similarly treated, the predominant reaction, illustrated in Figure 5.5.7, was photoionization followed sequentially by radical formation.(26)

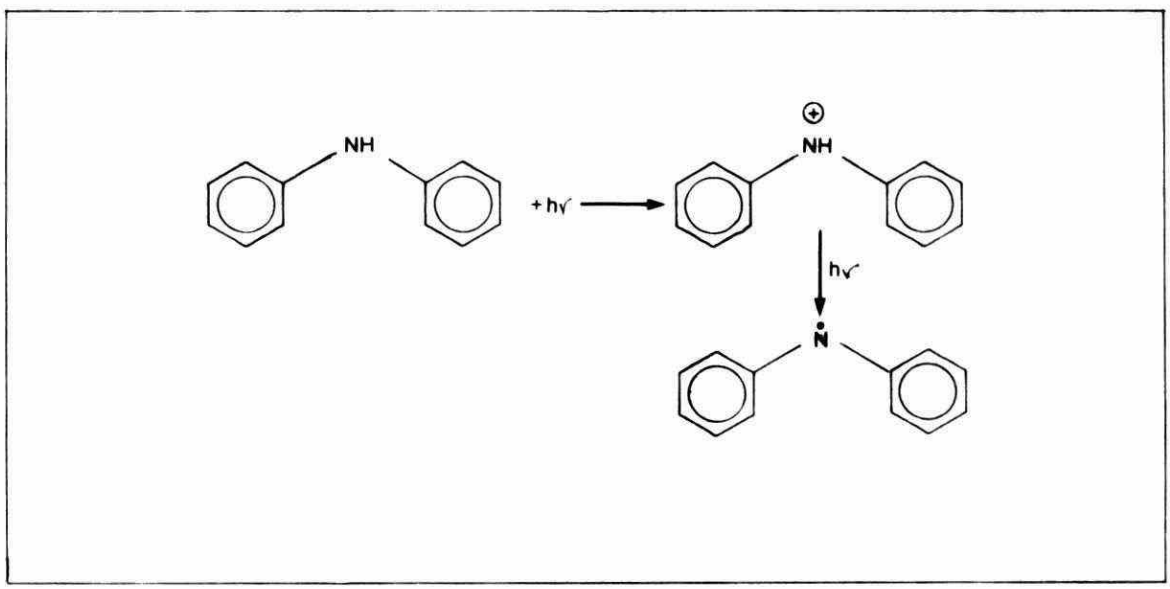


Figure 5.5.7 PHOTOLYSIS OF DIPHENYLAMINE

However, when an aryl-alkyl diamine, N,N,N',N'-tetramethyl-p-phenylenediamine, illustrated in Figure 5.5.8 was photolysed at low temperatures, fluorescence and phosphorescence were observed in addition to photoionization.

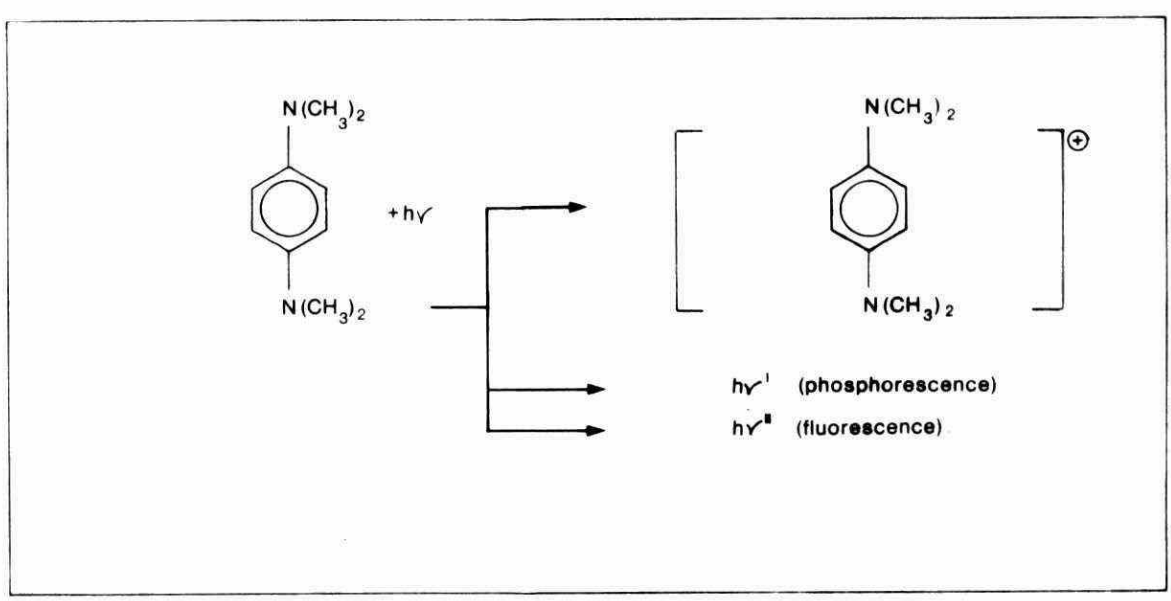


Figure 5.5.8 PHOTOLYSIS OF A DIALKYL AROMATIC AMINE

Similarly, with beta-Napthylamine, fluorescence and some deprotonization was observed. These reactions are illustrated in Figure 5.5.9.(26)

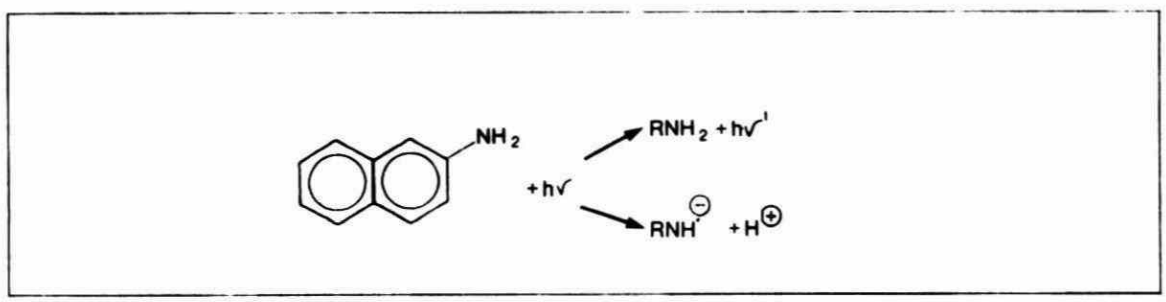


Figure 5.5.9 PHOTOLYSIS OF β NAPHTHYLAMINE

These general reactions are significant in that they suggest that the ionized or free radical species formed by photolysis can react further with other substrates.

Aromatic photonucleophilic substitutions are known to be particularly facile processes for compounds with halogens meta to hydroxyl, amino or methoxyl groups.(27) In water for example, the meta chlorine of pentachlorophenol is preferentially replaced by hydroxyl.

In a recent work, 3,4-dichloroaniline was photolyzed in water to yield 2-chloro-5-aminophenol.(28) This reaction appeared particularly facile, and it is suggested that the mechanism illustrated in Figure 5.5.10 is general for aromatic compounds having an electron donating substituent and a good leaving group in the meta position. This reaction could be of great significance in the free environment.

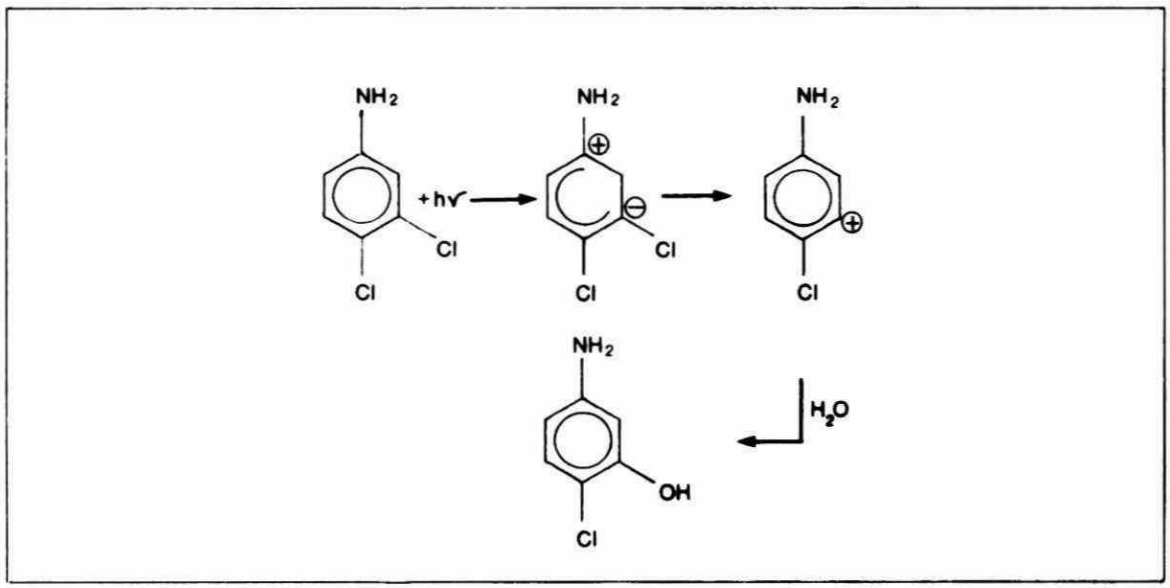


Figure 5.5.10 PHOTOLYSIS AND META-HYDROXYLATION OF CHLOROANILINES

5.5.4 Photolysis of Dyes

Aromatic azo compounds have received only limited attention from interested researchers. Attempts to identify photodegradation products or mechanisms are rare and have met with limited success. However, the available data, as in the case of aromatic amines, are instructive in establishing a base for further study.

When the simplest aromatic azo compound is irradiated, it normally undergoes a simple cis-trans transformation.(29) However, if the radiation is sufficiently intense and of sufficient duration, reductive cleavage(30) and ring cross linking have been observed.(31) These reactions are illustrated in Figure 5.5.11. These reactions are in contrast to those observed in dialkyl azo compounds, where carbon-nitrogen bond cleavage occurs with the liberation of free nitrogen.

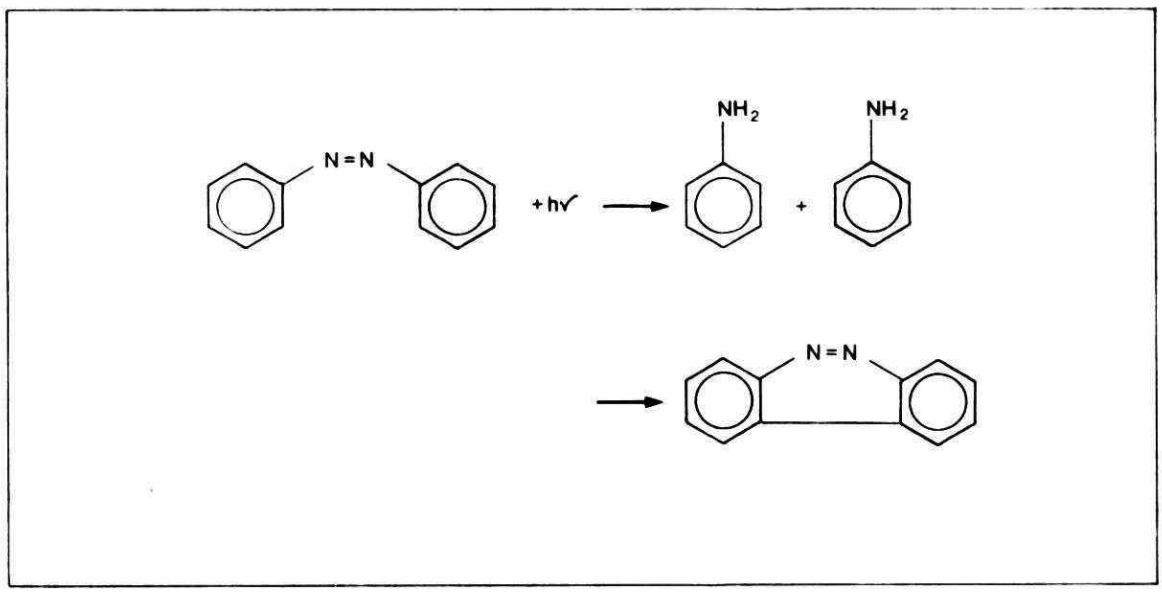


Figure 5.5.11 HIGH INTENSITY PHOTOLYSIS OF AZOBENZENE

In one recent study, an azo dye was irradiated in the presence of oxygen and the primary reaction product isolated, illustrated in Figure 5.5.12, was the azoxy compound. However, this product was reported to represent only 35% of the total reaction products.(32) The material balance was not completed, and other reaction products were not identified.

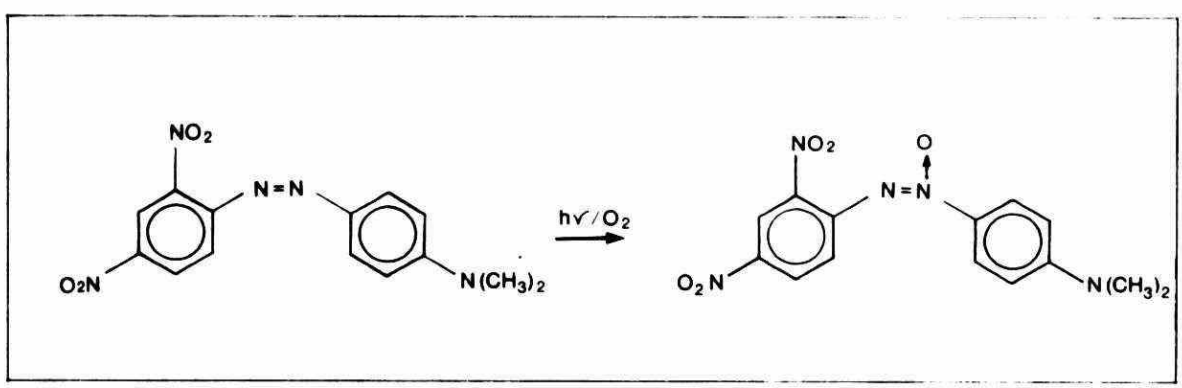


Figure 5.5.12 PHOTOCHEMICAL OXIDATION OF AN AZO DYE

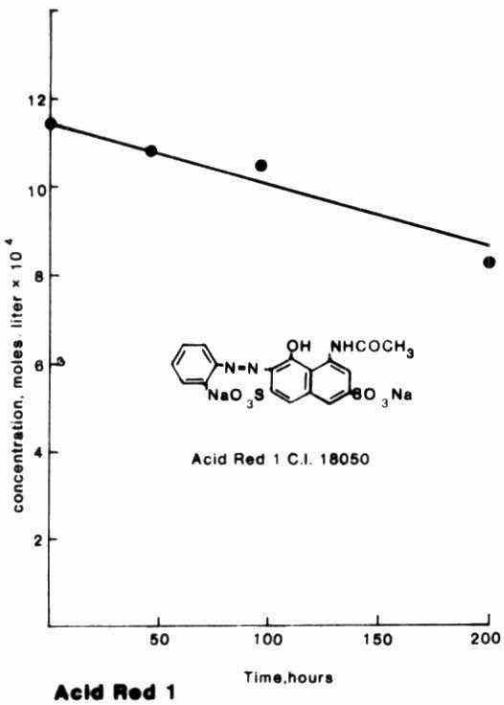
A number of azo dyes were subjected to photolysis in an effort to determine their rate of decolourization under intense irradiation.(33)

The source of radiation for these experiments was a carbon arc, which gave very high intensity radiation. Using this source, the reaction time was considerably reduced. As a control, some dyes were also exposed to natural sunlight; by this means it was confirmed that similar results were obtained, but over widely differing periods of time. For example, when direct blue 76 was irradiated with an arc lamp, it showed considerable decolorization after 250 hours. However, when a similar solution was exposed to natural sunlight, only a small portion of the dye was depleted after 1700 hours. These results are satisfactory validation of the tests.

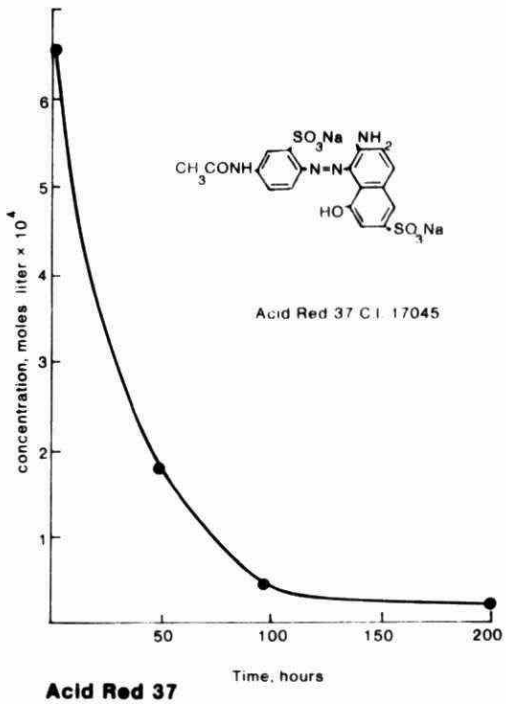
The overwhelming proportion of dyes photolyzed showed negligible decolourization even after some 200 hours of intensive radiation. However, a few were seen to react relatively rapidly. In consideration of this, Figure 5.5.13 presents for comparison the depletion curves for two representative examples of resistant dyes and two photolabile dyes.

The structural features required for photolability are not obvious from a cursory examination of the dyes. In fact, those decolorized and those showing resistance are quite similar in structure.

The decolorization observed may be due to reaction of the dye with singlet oxygen to form an oxidation product, as suggested in Figure 5.5.12. The particularly photolabile dyes might be particularly efficient oxygen sensitizers, however, this contention is purely speculative since no reaction products were identified.



Acid Red 1



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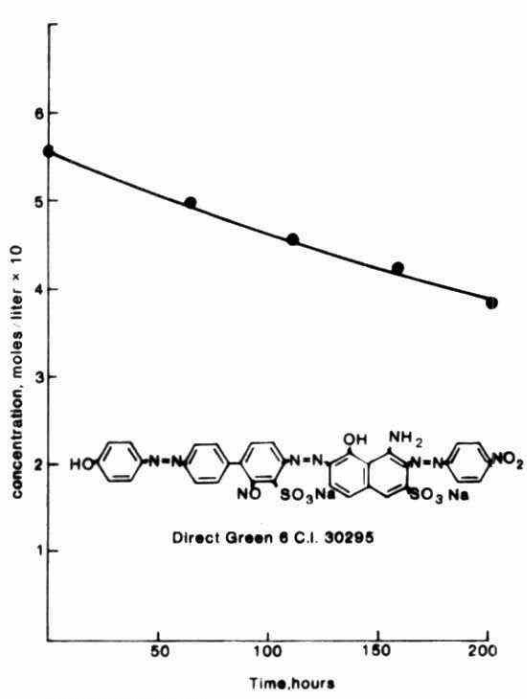

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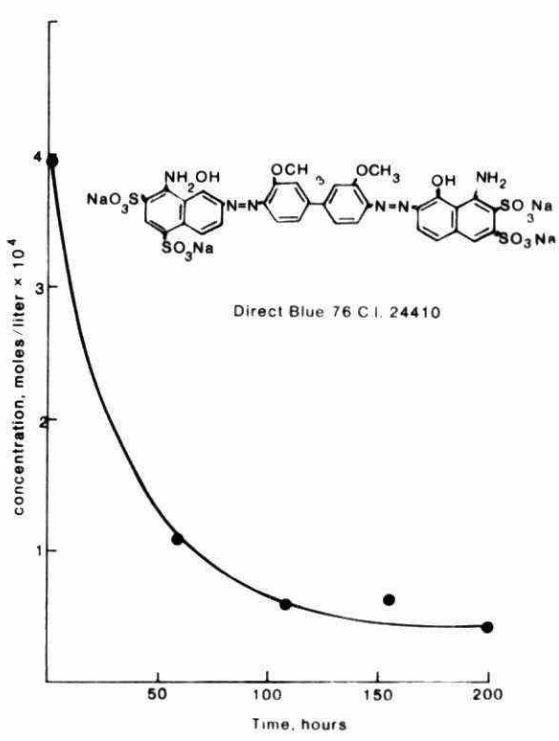

Direct Blue 76

Figure 5.5.13 RATE OF PHOTODEGRADATION OF SOME DYES IN WATER

5.5.5 Photolysis in the Natural Environment

"Environmental" photochemistry differs from classical "laboratory" photochemistry in several important ways, although the principles remain the same. There are several restrictions on light energy, both in wavelength range and intensity. The reagents are limited and concentrations are normally very low.

The specific chemical environment is extremely important, and the reaction pathway may be dramatically altered by relatively minor changes in environment.

The information uncovered relating to aromatic amines or azo dyes suggests that they are resistant to photochemical degradation, and consequently will have long environmental half lifes with respect to photolysis.

SELECTED INDUSTRIES AND EFFLUENTS

6

6.1 INTRODUCTION

This chapter deals with the industries most heavily involved in either the production or use of either aromatic amines or azo dyes. They have been selected on the basis of volume of use and potential for environmental impact.

Quantitative information relating specifically to the discharge of either aromatic amines or azo dyes in Ontario is generally not available. Consequently, information has been gathered from standard reference sources and related to the Ontario situation.

Each section gives a brief description of the appropriate process, with the objective of providing a working background. This background is subsequently utilized in specifying the source of emissions. The final sections provide a brief qualitative description of the quality of the effluents.

6.2 RUBBER CHEMICALS

6.2.1 Introduction

Antioxidants are organic compounds which show a propensity for oxidation and consequently, can be used to slow oxidative degradation of carrier materials. Desirable features of an antioxidant include: effectiveness at low concentrations, nontoxicity, inexpensiveness and ease of handling.

Antioxidants occur naturally in many plant species and serve as part of their natural defence system, as in natural rubber, which contains antioxidants.

Most elastomeric materials undergo deterioration, the rate of which depends on both their molecular structure and environmental factors. Oxidation of a rubber product is particularly undesirable because it induces changes in physical properties such as tensile strength, compression set, rebound and hardness. Oxidation of vulcanized rubber is manifested in three ways: (a) cross-linking; resulting in loss of elasticity, (b) chain scission; resulting in soft, weak, reverted rubber, (c) oxidation of the polymer to give oxygen-containing groups; such as ketone, alcohol or carboxyl functionalities.

6.2.2 Synthesis of Antioxidants

As indicated in a previous chapter, considerable quantities of aromatic amine antioxidants are synthesized in Ontario.

However, these processes are proprietary and the manufacturers are understandably reluctant to reveal their methods. However, the general literature describes many reactions which could be commercial synthetic routes. Some illustrative examples which may well be applicable to manufacturing in Ontario have been selected.

The primary starting materials in most aromatic amine rubber chemicals are aniline and diphenylamine. These compounds are nitrated, probably utilizing the classical nitric acid process. After reduction the diamine is obtained as illustrated in Figure 6.2.1.

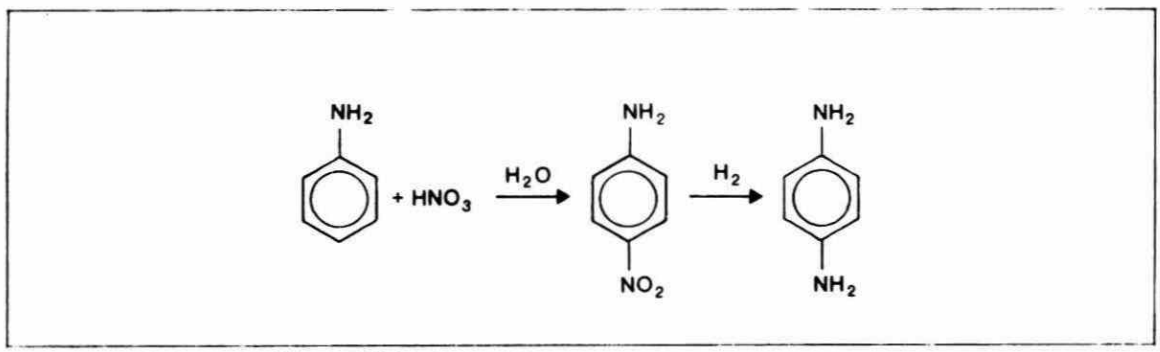

Figure 6.2.1 AMINATION OF ANILINE

The primary reaction involved in the synthesis of amine rubber chemicals is N substitution. In this substitution there are two choices, N-alkylation and N-arylation.

In N-alkylation, there are a number of possible routes which may be industrially applicable.

Utilization of a primary alcohol over a nickel catalyst as illustrated in Figure 6.2.2, yields the N-alkylated product in approximately 65% yield.(1) A similar high pressure reaction utilizing sulphuric acid as the catalyst, produces the N-alkylated derivative in high yields.

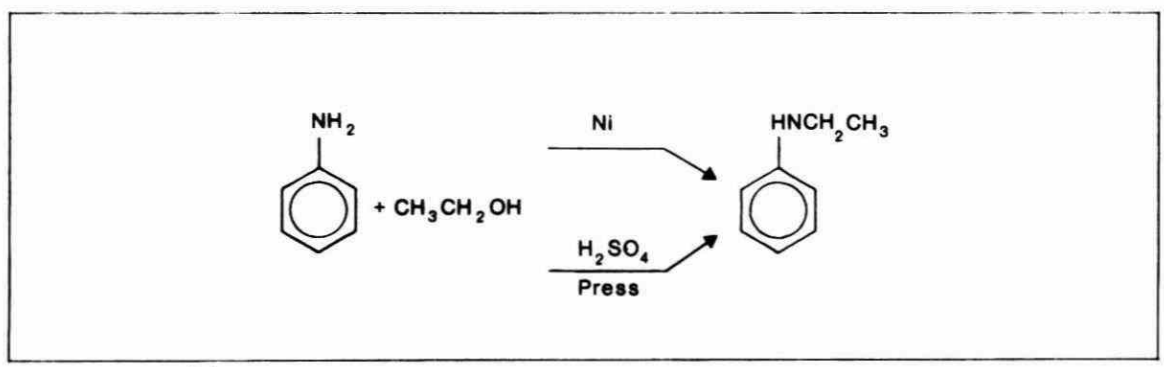

Figure 6.2.2 N-ALKYLATION OF ANILINE UTILIZING ALCHOLS

A more complicated reaction utilizing ketones as the alkylating agent has been reported. The reducing agent in this re-

action is sodium borohydride buffered in an ethanolic solution by acetic acid and sodium acetate. Yields for this reaction, illustrated in Figure 6.2.3, are greater than 90%.

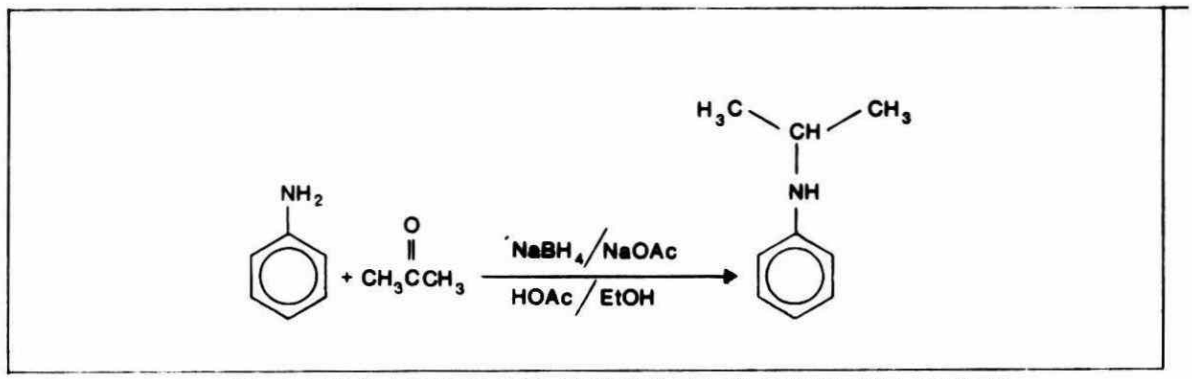

Figure 6.2.3 N-ALKYLATION OF ANILINE UTILIZING KETONES

The addition of an aromatic group to the amine functionality is somewhat more involved. The classical method for achieving this condensation is illustrated by the autoclave reaction of aniline and anilinehydrochloride in Figure 6.2.4. In this instance, the product is diphenylamine.(2) This reaction can be utilized to add an aromatic ring to many aromatic amines. This is the case in arylation of(p-amino-diphenylamine) to yield N, N'-diphenyl-paraphenylenediamine. This same product can be obtained in a reaction between aniline and p-hycroxy-aniline, in the process illustrated in Figure 6.2.5.

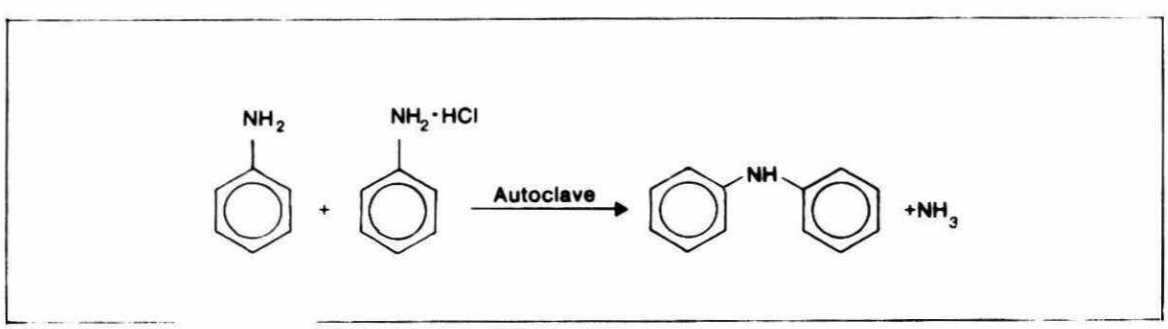

Figure 6.2.4 PRESSURE CONDENSATION OF DIPHENYLAMINE

There are, in addition, various other reactions which could yield the rubber chemicals produced in Ontario. However, the examples presented are considered representative.

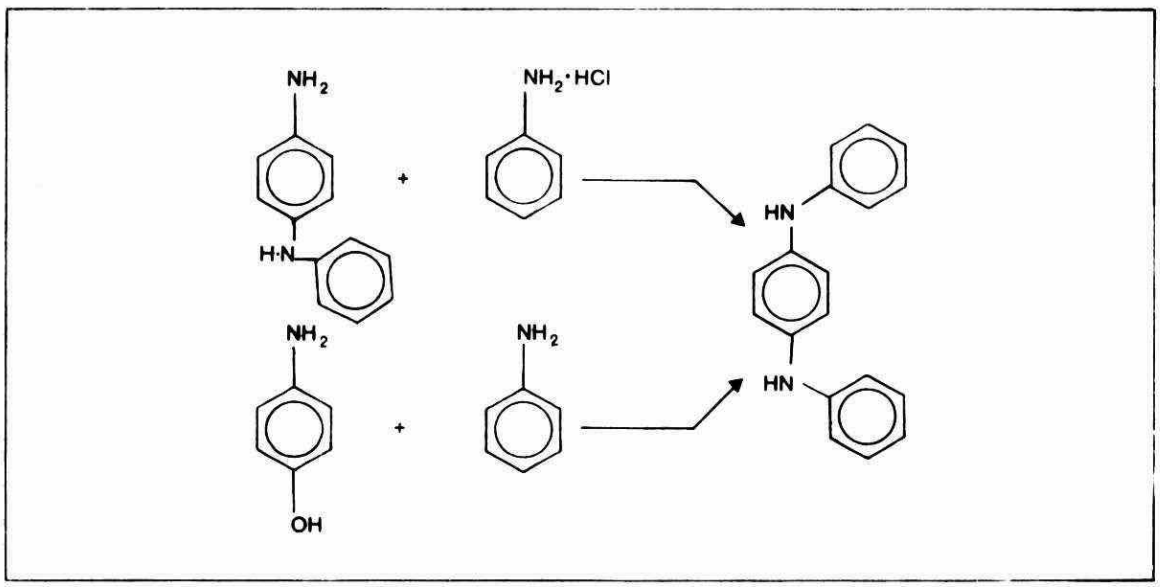

Figure 6.2.5 SYNTHESIS OF N, N'-DIPHENYL-PARAPHENYLENEDIAMINE

6.2.3 Mechanism of Action of Antioxidants

The mechanism of action for antioxidants in slowing the degradation of rubber is not clearly understood. However, the concensus is that a free radical quenching mechanism is involved.

The antioxidant is preferentially attached by an oxygen molecule, to form the antioxidant and hydroperoxide radicals. However, the oxygen can also attach the rubber molecule, to form a rubber radical. The choice of whether the oxygen reacts with either the rubber or the antioxidant is determined by kinetic factors and the specific properties of the antioxidant.

Once the radicals are formed, they react through the normal radical processes to form stable products. If the quenching

route yields a rubber hydroperoxide, the rubber will continue to degrade. However, if it reacts with either the antioxidant or a proton source, a stable product will result and the rubber degradation will be slowed.

Rate of rubber degradation is inversely related to the availability of free antioxidant. Over a period of time the antioxidant will be depleted in chain termination reactions and consequently will be unavailable for oxygen quenching. In this case, reacting oxygen will have no restraining factor preventing direct attack on the rubber.

6.2.4 Effectiveness of Antioxidants

The important rubber antioxidants may be divided chemically into two classes: amines and their derivatives, and phenols and their derivatives. The power, as antioxidants, of members of each class is approximately the same, but essential differences lie in their effectiveness in the presence of carbon black and in the degree of staining imparted to vulcanizates on exposure to light.

Consequently, the amines are used mostly in darker coloured rubbers where staining is not a problem. Conversely, the phenolics are used more in lighter coloured rubbers where aesthetics are more important.

As an illustration of the effectiveness of some aromatic amines, it is instructive to note their half lives with respect to oxidation. Of the phenylenediamines, the dioctyl derivative has a half life of eleven hours, the diphenyl is 134 hours and the alkyl-phenyl derivative is 34 hours.(3)

6.2.5 Emissions from Antioxidant Manufacturing

Since no specific information is available describing the processes used in aromatic amine synthesis, it is difficult to describe the effluents expected from these operations.

However, a qualitative overview may be valid, based on the speculated synthetic reactions previously described.

Since it is expected that most of the reactions occur in sealed vessels, it seems unlikely that significant emissions would be detected while a reaction is progressing.

However, when the reaction vessel is opened for product removal, it seems likely that volatile materials could escape into the atmosphere. This is particularly likely to occur when depressurizing heated autoclaves. The excess atmosphere is discharged to the outside environment and may carry aromatic amines.

In Ontario, some plants discharge aqueous wastes into the sewerage system with the result that aromatic amines pass through the Municipal sewage plants. This method of waste disposal has been practiced for many years, however, the effectiveness of municipal treatment on amine depletion is questionable.

The aqueous discharges will likely contain quantities of all the products manufactured plus starting materials, catalyst and solvents.

6.3 MANUFACTURE OF RUBBER PRODUCTS

6.3.1 Introduction

The rubber industry involves the production of raw materials, monomers, synthetic rubbers, importation and purification of natural rubber, the production of rubber chemicals, additives, and the manufacture of rubber products.

The commercial application of raw rubber is, with a few exceptions, very limited. These are restricted to adhes-

ives, sealants, friction and electrical tapes and crepe rubber for shoe soles. In the majority of cases, to produce a commercial material, the raw polymers must be modified by the addition of chemicals. This is followed by forming and vulcanization to produce the desired rubber product.

6.3.2 Synthesis of Rubber

Rubber occurs in some plants as sap. It has the appearance of a milky latex, and only two sources are commercially important at present. The first is the Hevea Brasiliensis tree grown throughout the tropics and the Kok Saghys, a dandelion grown primarily in Russia.

The dry product is obtained by precipitation and coagulation, during which the latex is destabilized through the addition of acids and salt. Latex is highly sensitive to bacterial action, therefore preservatives are added to sterilize and provide protection during shipment.

The natural rubber molecule, cis-polyisoprene, has been duplicated by catalytic polymerization of isoprene. The synthetics have largely replaced the natural product, however, it still is important in specialized applications.

Synthetic rubbers, also known as synthetic elastomers, are a group of polymeric materials with properties resembling that of natural rubber. The major process routes for synthetic rubber production are emulsion and solution polymerization. The main difference between the processes being the solvent system which affects the physical state of the monomers.

Emulsion polymerization may be viewed as polymerization of droplets suspended in water. Solution polymerization may be viewed as polymerization in which excess monomer serves as a solvent.

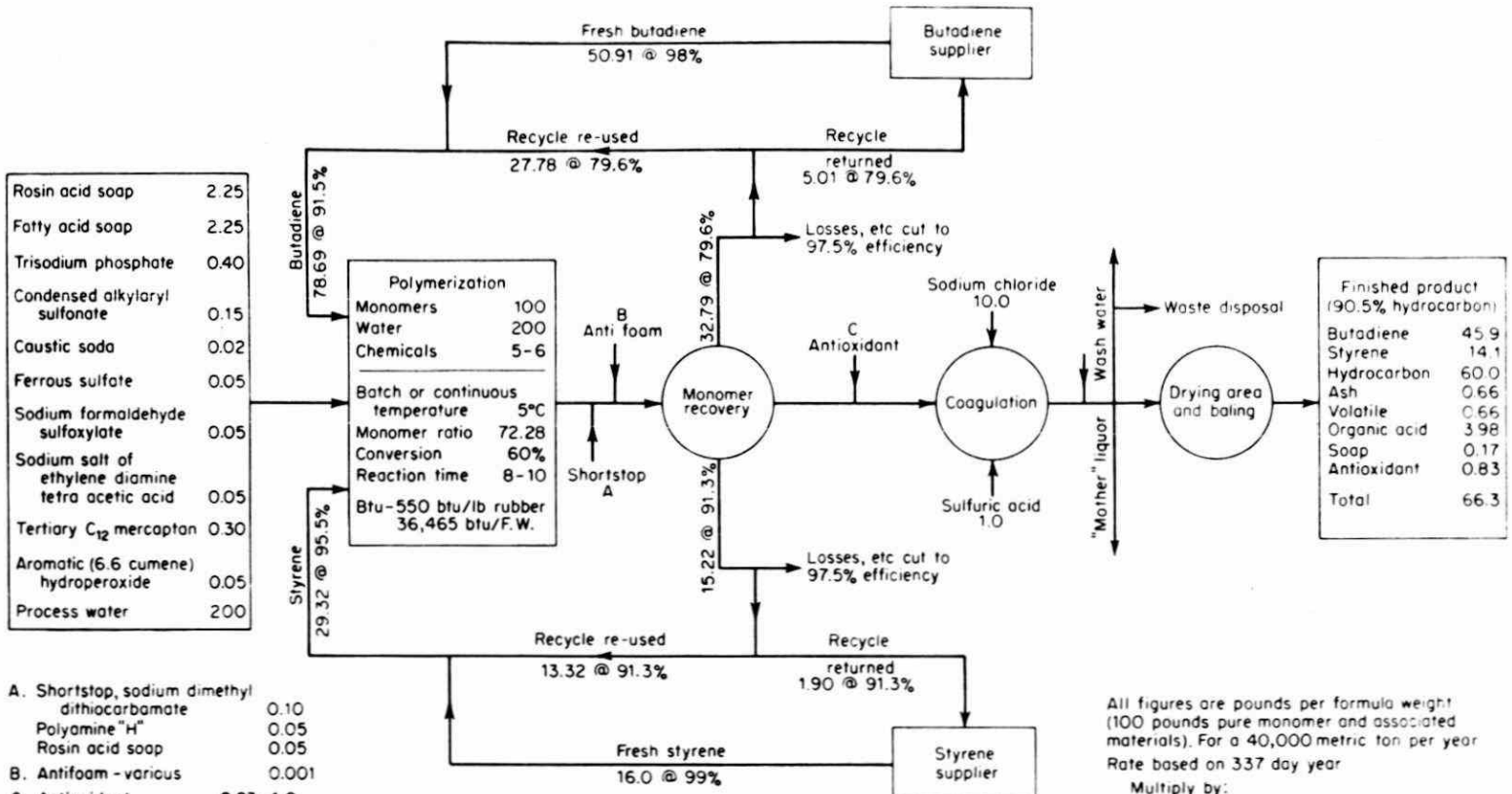

Figure 6.3.1 FLOW DIAGRAM FOR RUBBER SYNTHESIS

(Source: Shreve)

In a typical emulsion system, the monomer is mixed with an emulsifier, catalyst and modifying agent, while suspended in water. Heating under agitation in a pressure vessel achieves the desired conversion. When the desired degree of polymerization is achieved, the reaction is stopped and the emulsion is stripped of unreacted monomer. Antioxidants are added and the rubber is isolated from the latex emulsion by coagulation with acids and inorganic salts (see Table 6.3.1).

The principal types of elastomeric polymers commercially available from emulsion polymerization systems are butadiene-styrene, butadiene-acrylonitrile, terpolymers of butadiene-acrylonitrile and styrene, and chloroprene.

The flow chart given in Figure 6.3.1 shows the material balance for a typical styrene-butadiene rubber (SBR) plant. Several synthetic rubbers can be made in a normal rubber plant.

6.3.3 Compounding of Rubber Products

Synthetic rubber requires fillers and curing. The essential steps in rubber fabrication are mixing, forming and vulcanizing. These processes are collectively termed rubber compounding.

Compounding chemicals are used in rubber for the purpose of facilitating the fabrication of and the improvement of the quality of rubber products. The type and concentration of the various ingredients that make up a rubber compound depend on the properties desired in the finished product. A brief description of the principal rubber chemicals is presented in Table 6.3.1. The ingredients of typical rubber compound are extracted from Shreve and shown in Table 6.3.2.

TABLE 6.3.2

TYPICAL COMPOSITION OF PROCESSED RUBBER

Ingredients	Parts By Weight
Rubber	100.0
Sulfur	2.0
Zinc oxide	5.0
Stearic acid	3.0
Accelerator	1.5
Pigments	50.0
Reclaimer, softeners, extenders, antioxidants, antiozonates, etc.	8.0

The first step in rubber compounding is mastication. This is the process in which mixing of raw polymer and fillers, processing aids, curatives, antioxidants and softeners is achieved. Mastication is performed either in a roll mill mixer or in a closed mixer such as the Banbury. The roll mill consists of two parallel, horizontal rolls rotating in oposite directions which give the desired degree of mastication rapidly. The Banbury mixer is an enclosed machine containing two water cooled rotors operating in a water cooled chamber. Considerable heat is generated during mixing and must be dissipated and controlled.

In general, the rubber chemicals such as zinc oxide, antioxidants and stearic acid are added first, followed by carbon black and softeners.

The second phase comprises the mixing in of all other chemical ingredients; the accelerators and vulcanizing agents being added last. Mixing is continued until a uniform blend of all constituents has been achieved.

TABLE 6.3.1

PRINCIPAL CHEMICALS USED IN COMPOUNDING RUBBER

Antioxidants - N-Phenyl-2-naphthylamine, alkylated diphenylamine, acetone-diphenylamine reaction product, other aromatic amines and phenols.

Vulcanizing, or curing, agents - Sulfur, sulfur monochloride, selenium, tellurium, thiuram disulfides, p-quinone dioximes, polysulfide polymers.

Vulcanization accelerators - 2-Mercaptobenzothiazole, benzothizolyl disulfide, zinc diethyldithiocarbamate, tetramethylthiuram monosulfide, 1,3-diphenyl-quanidine.

Accelerator activators - Zinc oxide, stearic acid, litharge, magnesium oxide, amines, amine soaps.

Retarders - Salicylic acid, benzoic acid, phthalic anhydride.

Pigments - Carbon black, zinc oxide, certain clays, calcium carbonate, titanium dioxide, colour pigments.

Softeners and extenders - Petroleum oils, pine tars and resins, coal-tar fractions.

Waxes - Petroleum waxes.

Blowing agents - Sodium or ammonium bicarbonate, diazoaminobenzene, dinitrosopentamethylene-tetramine.

Chemical plasticizers - 2-Naphthalenethiol, bis(o-benzaminophenyl)-disulfide, mixed xylenethiols, zinc salts of xylenethiols.

Peptizers - Aromatic mercaptans (thiophenols).

Prior to final vulcanization, the blended stock must be formed into the desired shape. This is achieved either by calendering or extrusion. Coating operations are performed on calendering machines whereas hose, inner tubes, tire treads and such articles are fashioned by extrusion.

Vulcanization is an irreversible process during which the rubber compound, through a change in its chemical structure, becomes less plastic and gains other desirable physical properties such as elasticity, toughness, hardness and impermeability.

6.3.4 Emissions From Rubber Compounding

Emissions to both air and water can occur from any of the stages in rubber synthesis or compounding. Aromatic amines may be discharged as distinct entities from the mixing stage, but can also be found as components in emissions from subsequent stages. Consequently, it is relevant to review the general sources and qualities of pollution produced by rubber compounding. Aromatic amines should be considered as integral to the general emissions.

The characteristics of emissions from rubber compounding will vary, depending on the specific product manufactured. However, the compounding and manufacturing of auto tires can serve as a good illustration.

Raw waste water discharged from a tire plant contains colloidal suspensions containing latex, soap, oil and other emulsions that impart both turbidity and oxygen demand. Additionally, other materials present include particles of rubber, talc, lime and carbon black which exist as a very fine suspension.(5)

Biological oxygen demand (BOD) may range in value from 1 mg/L to 30 mg/L for process waste water. However, these ranges may be higher in instances where sanitary wastes are combined with process waters.(5)

The chemical oxygen demand (COD) from tire compounding is attributable principally to washdown and runoff from oil contaminated soapstone and latex drip areas. The COD values generally will range from 5 mg/L to 30 mg/L.(5)

Suspended solids may come from any of the process operations, and values are found to vary between 10 mg/L and 20 000 mg/L, depending on the effectiveness of in-plant controls, and the effect of shock loading when soapstone solution is dumped.(5)

Oil and grease exist in process waste waters due to washdown, runoff, spills and leakage in the process areas which pick up lubricating oil from machinery and extender oils from various locations. Concentration values in the total effluent range from 5 mg/L to 83 mg/L. Since oily wastes usually result from intermittent flows, instantaneous values may be much higher.(5)

Heavy metals have been detected in rubber plant effluents in concentrations ranging from 50 ppb for chromium to 2000 ppb for iron.(6) These values were recorded on effluents after treatment, however, no corresponding values were recorded for the raw effluent.

Airborne emissions can occur during the blending operations. Oil and dust can escape from the dust seal rings on Banbury mixers and result in air discharges which might carry aromatic amines.

A second source of air emissions occurs during tire grinding and polishing operations. The base surface for white wall tires is prepared by abrasive grinding. Similarly, surface flaws are removed by abrasive polishing. Consequently, an airborne rubber dust results. This dust is usually directed to baghouses for collection, but some may escape into the outside environment.

6.4 THE PULP AND PAPER INDUSTRY

6.4.1 The Production of Pulp

Pulp is the fundamental feedstock for the production of paper. It is generally obtained from the processing of trees, but in more recent years, recycling operations have resulted in the reuse of paper fibres and cloths.

The overall generalized pulp making process is illustrated in Figure 6.4.1; the bulk of information in this section is due to MacDonald.(7)

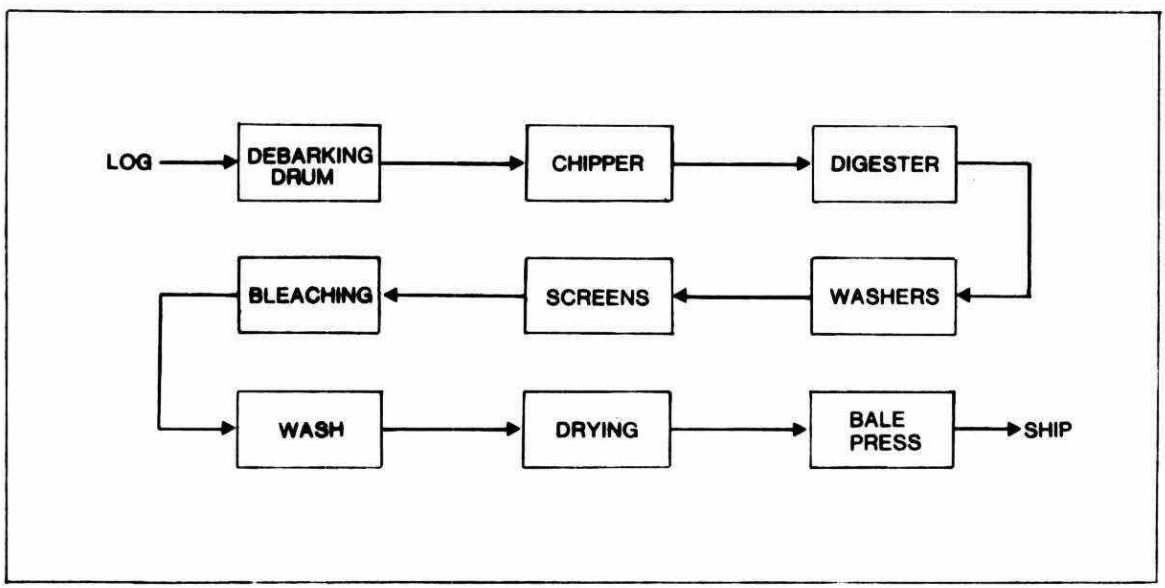

Figure 6.4.1 MANUFACTURE OF PULP

The first steps in pulp making are tree debarking (with high pressure hoses or in a rotating drum), chipping, and screening.

The wood chips are then transferred to a digester. This is a reaction vessel in which the chips are degraded chemically to separate the cellulose fibres from undesired materials such as lignin and miscellaneous organic tars. There are

two main methods currently employed to facilitate this process: the kraft process; and the sulphite process. For the purposes of the report, the differences are related to the treatment chemicals used.

The crude fibres are transferred to the blow tank where they are held in preparation for washing.

In the washing stage, a series of machines is utilized to rinse the fibres until a consistent state of cleanliness is achieved.

Following washing, the clean fibres are passed through a series of filters which serve to remove wood knots and lumps of coagulated fibre.

Subsequent to screening, the fibres are bleached to improve colour and appearance. Additionally, a bleached product facilitates dyeing in subsequent stages.

The bleached fibre is then subjected to washing, concentrating and drying, where most of the water is evaporated.

Finally, the dry fibre is compacted in a bale press. Here, it is baled and packaged for either transportation to the paper mill or, in an integrated plant, moved on to the paper making process.

6.4.2 Manufacture of Paper

Paper making can be performed either in a completely separate plant or integrated with the pulping operation. The general papermaking process is illustrated in Figure 6.4.2.

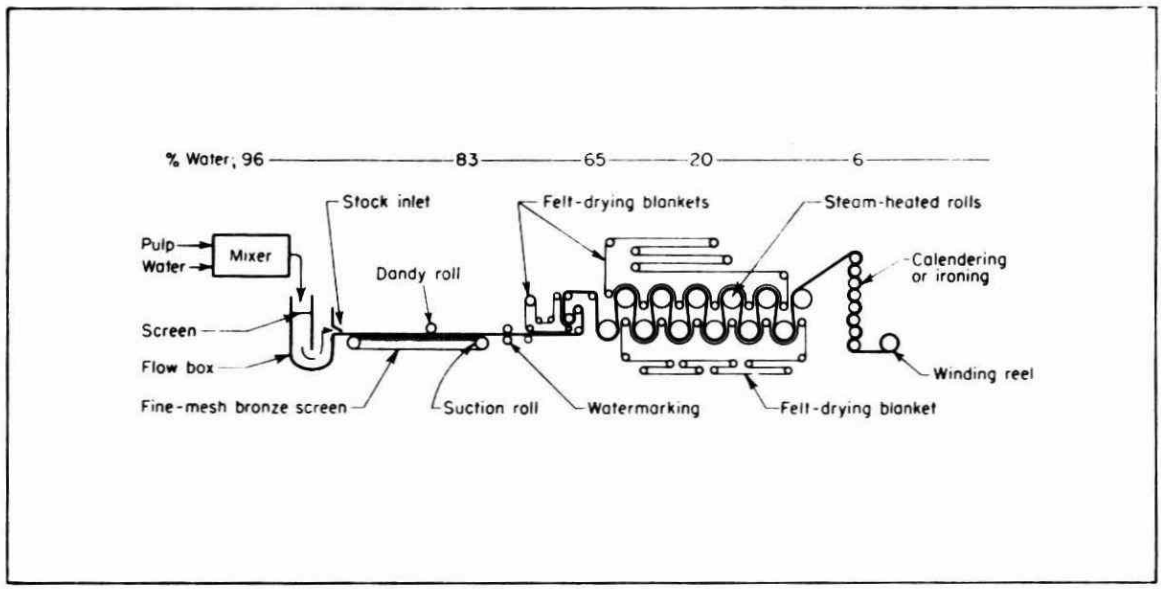

Figure 6.4.2 MANUFACTURE OF PAPER (Source:Shreve)

The pulp from the pulp mill is re-slurried in a large tank called "the beater". This stage subjects the pulp to violent agitation which flares the fibres and produces a homogenous slurry. This beating also serves to impart desirable physical characteristics to the final paper product.

This process vessel is also commonly used for the addition of chemical agents to the paper. These agents are added to assist in the production of a paper which meets defined specifications. This stage is one of two in which dye stuffs may be added.

The treated pulp then moves through the actual paper making machine. In our example, we have selected a Fourdrinier machine, however, the essential principles remain the same in most machines.

The actual paper is made by a process of spreading down a uniform layer of fibre slurry onto a fine mesh screen. The fibre layer is subjected to a vacuum which withdraws the water and causes the fibres to mat and form a cohesive sheet.

Subsequent stages of vacuum filtration and drying result in a sheet of paper.

This sheet of paper is continuously withdrawn and after passing through a series of smoothening rollers known as "the calender stack" is wound into a roll.

The rolling stage is the final stage in paper making and the product moves from here to the marketplace.

6.4.3 Colouring of Paper

Dyes and coloured pigments are added to paper for two reasons: to produce a definite coloured paper; or to produce a uniformly coloured product such as in "white" paper. Natural fibres, even after bleaching, have a distinct yellowish tinge. Consequently to produce white paper, dyestuffs must be added.

There are three main methods utilized in paper colouring:

(a) pulp colouring
(b) surface colouring
(c) tub and vat dyeing

It is not unusual to find combinations of methods or to find individual variations in the specific process stage in which the dye is added. However, pulp colouring appears to be the most common.

Pulp dyeing is often a continuous process. In this method, a metered quantity of dye is added to the pulp in the beater. The coloured pulp then moves through the stages previously described in the paper making process.

An illustration of a continuous dyeing process is presented in Figure 6.4.3. In this illustration, the dyes are blended in concentrated solution on the first level of the building. This solution is transferred to dilution and surge tanks located on a second level, where it is held in readiness.

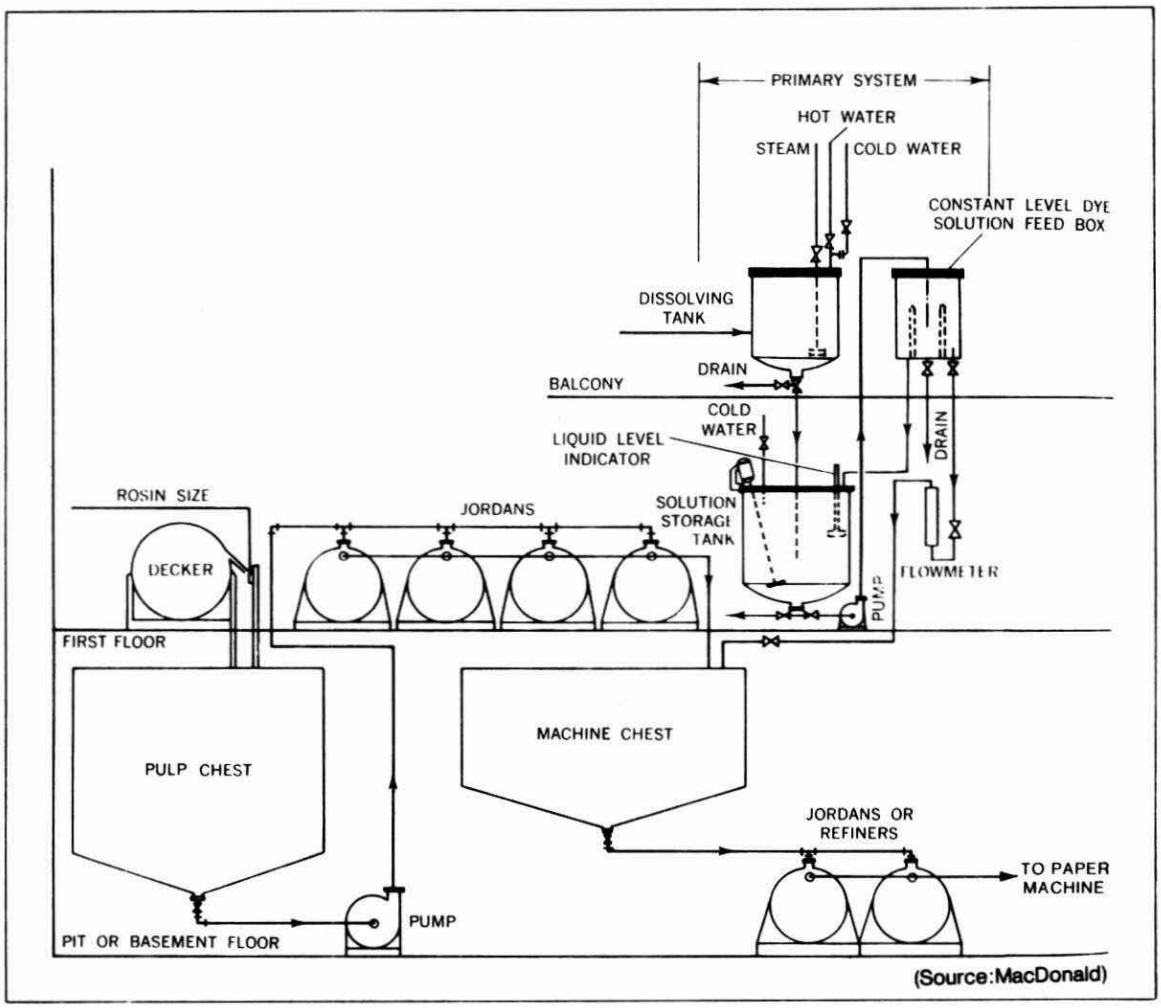

Figure 6.4.3 FLOW DIAGRAM - CONTINUOUS COLORING OF PAPER

The dye is actually added to the pulp in the pulp slurrying tank. In between stages there are storage tanks which act as surge barriers, and retention tanks designed to aid the dyeing and paper making process.

Surface colouring can occur in the paper making machine but is more commonly encountered in the calender stage. In calender dyeing, illustrated in Figure 6.4.4, the dye solution is stored in containers called "colour boxes". The dye trickles out of these boxes onto the rollers, which transfer the colour to the paper being pressed between them.

Two related types of dyeing which are occasionally encountered are "tub dyeing" and "vat dyeing". In tub dyeing the nearly finished sheet of paper is passed through a vat of dye solution. After drying the finished product is rolled and shipped.

Vat dyeing is usually a small scale operation in which specialty papers are cut and dyed to order. This method requires that the sheet of paper be dipped in a vat of dye.

6.4.4 Sources of Dyestuff Discharges

The greatest source of dyestuff emission is the discharge from filtration of the pulp in the Fourdrinier machine. Referring to Figure 6.4.2, it can be seen that the vacuum filters under the mesh screen withdraw much of the process water, which is also the dye carrier.

In some cases, this filtrate is recycled, however, in most cases, it is discharged from the plant.

Additional dyestuff discharge will occur from the pulp slurrying tanks and the dyestuff mixing tanks. This is particularly true when a change is made in the colour being used or the equipment is being cleaned.

The waters resulting from the drying stages are most likely to be in the vapour phase, and consequently, unlikely to contain significant quantities of dyestuffs.

In calender dyeing, wastes will occur when dye solutions drip off the rollers or the paper into waste containers which discharge the dye from the plant. These drippings are in some instances recycled. The colour boxes may become contaminated and render the dye solution unsuitable. In that case, the solution is discarded.

Waste waters result every time a machine is cleaned. Dye solutions are dumped when they become contaminated or a colour change is desired. Similarly, drippings from dyed papers will be discharged from the plant.

The calenders can be a source of air discharges. The rotation of the rollers in the dye solution can result in a fine aerosol mist being discharged into the air.

Vat and tub dyeing both yield dyestuff discharges when undesired solutions are dumped.

No information quantifying dyestuff pollution as a component distinct from general pollution was uncovered. However, a general statement on pollutant colour can be made.

Typical colour value for bleached kraft mill effluent is in the order of 2000 APHA units, caustic extract has a value of 20 000 APHA units. For comparison, Coca-Cola has a APHA value of 8500 units, while draft beer is 1000 units.(2)

Consequently, it seems clear that in terms of the overall colour discharged from a pulp and paper operation, dye stuff pollution is a minor contributor.

6.5 TEXTILE INDUSTRY

6.5.1 Introduction

The textile industry is engaged in the processing of fibres to produce either personal garments, floor coverings or industrial cloths.

Textile wastes are generally coloured, highly alkaline, high in both BOD and suspended solids, and high in temperature. This industry has long been a major water user and dis-

charger. There has been little success in developing low cost treatment methods, which are urgently required to lessen the pollution loads discharged from textile plants.

6.5.2 Manufacture of Textiles

Textile products are manufactured from one or more of three fabric types: wool, cotton, or synthetics. Each of the fabric categories may undergo slightly different processing which can result in significant variability in the quantity and quality of textile plant effluents. The actual process operations carried out on a fabric will also depend on the end use and required characteristics of the textile.

Textile manufacturing can be divided into three segments: preparation of fibres, colouring of fibres, and the application of finishes.

Fibres received at the textile plant contain dirt, oils and grease or exhibit other properties which must be altered prior to colouring or manufacture of the finished textile product. The major fibre preparation operations are described in Table 6.5.1.

TABLE 6.5.1

PROCESSES USED IN PREPARING TEXTILES

Slashing	Application of a "size" such as polyvinyl alcohol, starch substitutes, carboxymethyl cellulose, etc. to cotton fibres to impart tensile strength before wearing.
Desizing	The removal of size from joints by hydrolysis with an acid or enzyme.

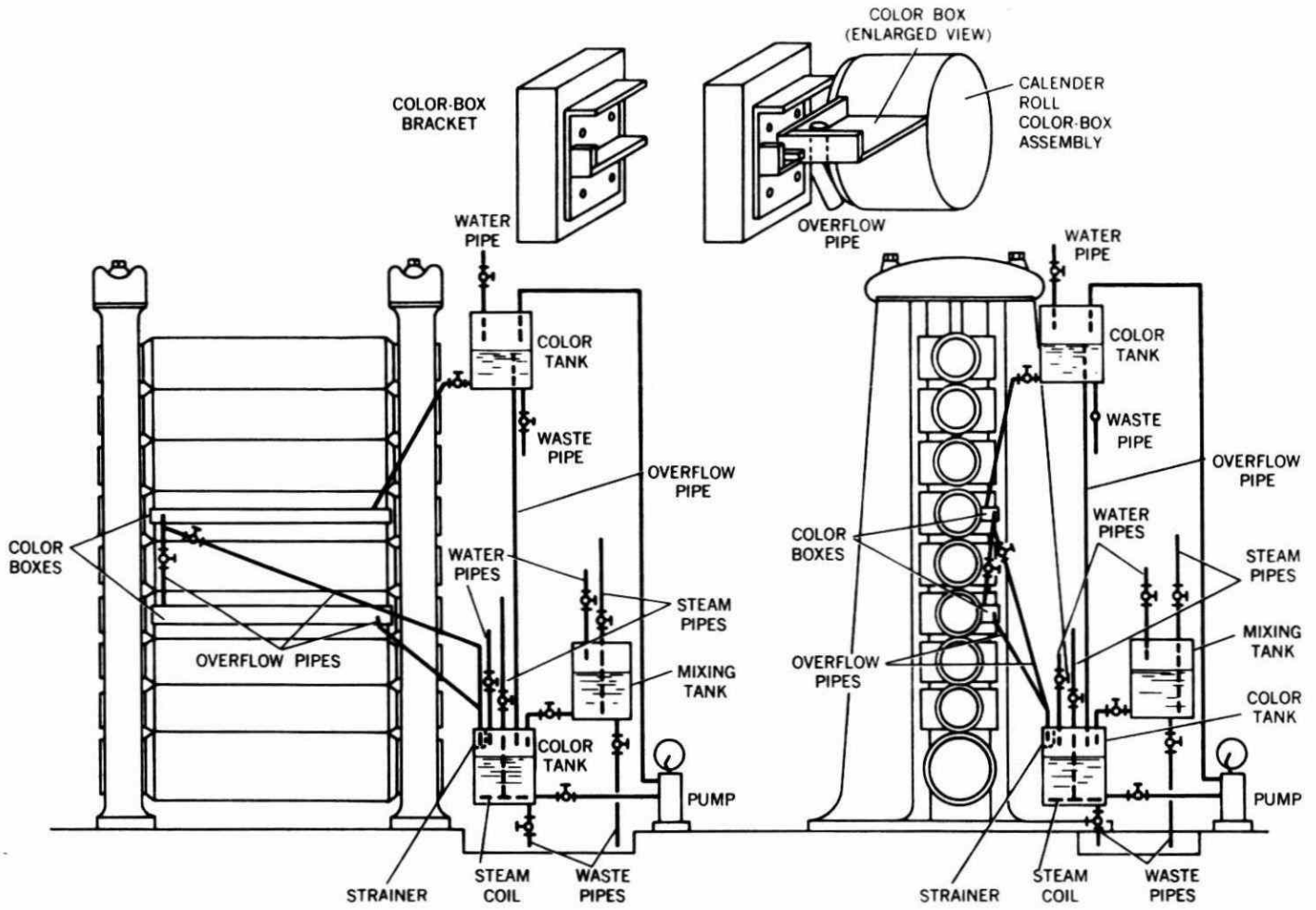

Figure 6.4.4 EQUIPMENT FOR CALENDER COLORING

(Source:MacDonald)

Scouring — The removal of grease, dirt, waxes with hot alkaline detergent and in some cases solvents.

Bleaching — The whitening of material or synthetic fibres generally with hydrogen peroxide or sodium hypochlorite.

Mercerizing — Washing of cotton fabrics in sodium hydroxide solution to improve lustre, tensile strength and dye affinity.

Carbonizing — The addition of mineral acid to wool fabrics to convert vegetable matter to carbon which can be mechanically removed.

6.5.3 Colouring of Textiles

Textile fabrics can be coloured by either of two fundamental processes: dyeing or printing. These processes differ in that dyeing requires penetration of the colourant into the fibre, while in printing, the colourant remains close to the surface.

Dyes are added to fabrics in combination with a variety of chemical agents which facilitate the process. These agents are usually surfactants, detergents, developers or other miscellaneous materials. Some of these are subsequently removed by washing and are found in plant effluents.

Dyeing can be achieved in either batch or continuous operations. The criterion for selection is most commonly based on the quantity of material to be coloured, and its physical nature. For example, nylon hosiery is most often dyed in batch baths, whereas carpets would be coloured in continuous operations.

One of the major differences between batch and continuous dyeing operations is the concentration of dyestuffs used. Batch operations generally are dilute solutions with high liquid to fabric ratios, whereas continuous operations use concentrated solutions with lower liquid to fabric ratios.

Another difference relates to process duration. Batch dyeing processes are often slow operations taking several hours to complete. Continuous dyeing processes are much more rapid than batch processes and in general tend to use highly sophisticated equipment.

The two most common types of batch machines are becks and jigs. Other batch machines include the keen, package, beam, hosiery and jet dying machines.

A dye beck is illustrated in Figure 6.5.1, in which a long continuous loop of fabric is drawn through a heated dyebath. In this case, the liquid to fabric ratio may be as high as 20:1.

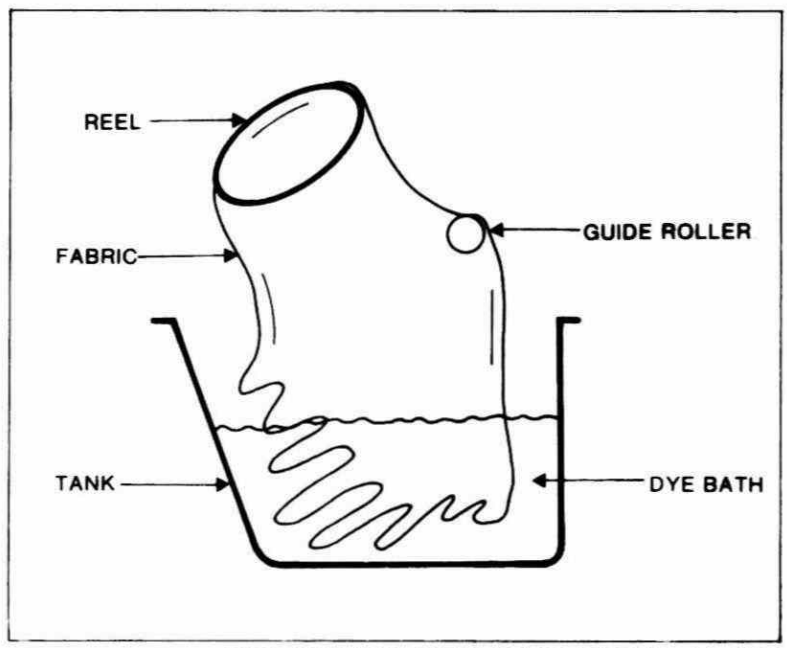

Figure 6.5.1 BATCH DYEING-DYE BECK Ref(8)

The dye jig operates in a similar fashion except that the fabric is constantly rolled back and forth between two rollers until the desired colour is obtained. In this process, the liquid to fabric ratio may be only 4:1.(1)

For the purposes of comparison, Figure 6.5.2 illustrates a hosiery dying bath. This process, utilized for batch dyeing of small articles, is very common in small dyeing operations.

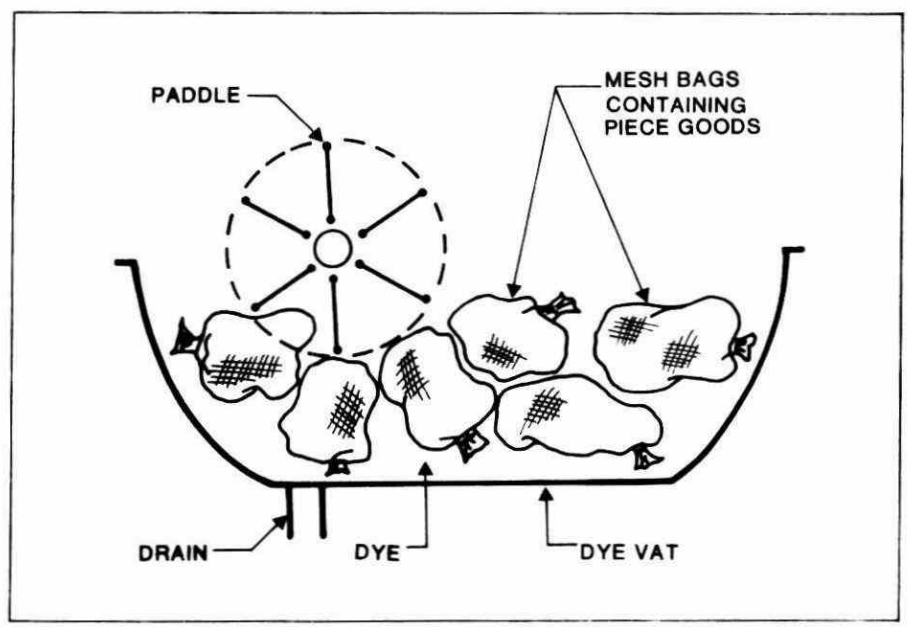

Figure 6.5.2 BATCH DYEING-HOSIERY DYEING Ref(8)

One continuous dyeing machine commonly used by the carpet industry in Ontario is the Butterworth-Kusters range illustrated in Figure 6.5.3. In this machine, the carpet is first wetted and surfactants and other chemicals added. A concentrated dye solution is then applied with the aid of rollers as the carpet moves through the machine; an even tone is achieved by mechanically spreading the dye. The carpet is subsequently steamed, washed, rinsed, dryed and rolled.

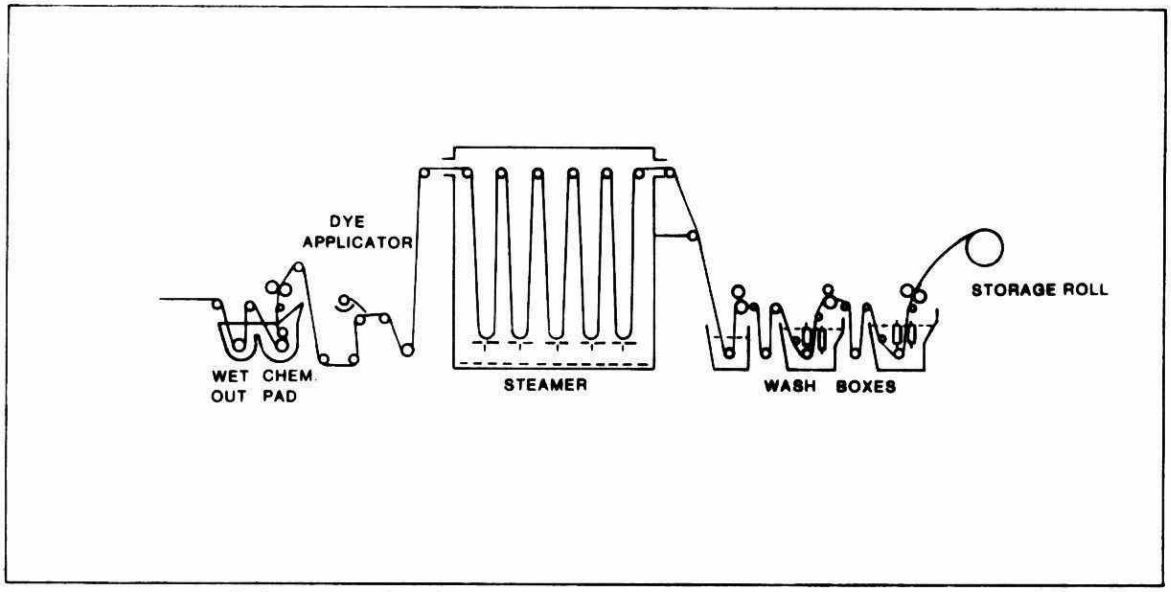

Figure 6.5.3 CONTINUOUS DYEING (BUTTERWORTH-KUSTER) Ref(8)

Other continuous dyeing machines include the pad steam machine, thermisol range and indigo dyeing range. The essential difference between these machines and the Butterworth range lies in the dye application. In these machines, the fabric is usually passed through a dye solution rather than have it rolled in from the surface.

Fabric printing operations are similar to the continuous dyeing process. Dyes are applied to one side of the fabric either by pressing the dye through silk screens or transferring it from rollers, as in paper printing.

The dyes are usually applied as thick pastes, a requirement that permits the printing of complex patterns.

6.5.4 Sources of Dyestuff Discharges

Textile operations use significant quantities of water and produce effluents which are high in BOD, suspended and dissolved solids, colour and oils. For illustration, Figure

6.5.4 presents a generalized flow diagram of a textile operation. Each major step is identified together with its usual waste characteristics.(9)

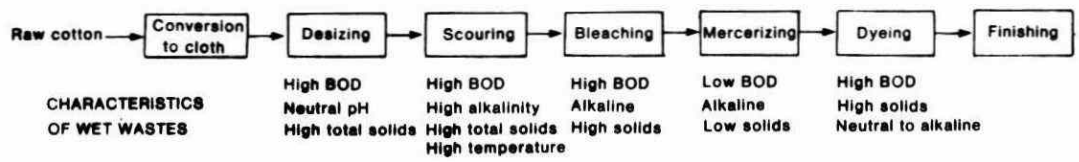

Figure 6.5.4 COTTON TEXTILE PROCESSING FLOW DIAGRAM Ref(9)

A more specific description of the wastes is presented in Table 6.5.2. Here, the specific processes are listed with their general ranges of pollution contribution.

The specific contribution relating to dyestuffs is broken down by distinct dye class.

The BOD contribution of the dyeing process ranges from 15% to 30% of the total pollution loading.(9) However, in a textile plant which does not engage in fibre preparation, the BOD from dyeing may approach 100%.

In general terms, batch processess tend to be more efficient in the utilization of dyes. However, there are great variations in the dye utilization which are dependent on both the specific dye used and the fabric dyed. Table 6.5.3 illustrates the variation in BOD for wastes from the different processes using different dyes.

Process	1b BOD/1000 1b cloth
Vat dye, continuous	18
Vat dye, jig	32
Naphthol, jig	14
Direct, jig	0.5
Sulfur, jig	31

Table 6.5.3 BOD CONTRIBUTED IN THE DYE PROCESS Ref(9)

The primary sources of dyestuff pollution are from exhausted dye baths, wash and rinse waters, equipment cleaning and spillage.

When a dye bath reaches a certain minimum in colour intensity or is excessively contaminated with foreign materials, it is normally dumped. Similarly, if a colour change is required, the unwanted solution is also usually dumped.

Equipment cleaning contributes a significant proportion of dye waste. This is particularly true in silk screen printing, where with each pattern or colour change, the screens are washed and all solutions dumped.

In the normal textile plant all dumped solutions are combined and discharged from the plant. In Ontario, the majority of textile operations discharge these wastes to municipal sewers or water bodies. As many textile operations are located in smaller towns, they may contribute significantly to the overall loadings to the treatment plant.

There are few plants in Ontario with their own treatment systems. In general, the existing ones tend to be biological treatment systems which have little effect on the colour due to dyestuffs. At least one plant has activated carbon treatment, and one other practices chemical precipitation.

TABLE 6.5.2

POLLUTION EFFECT OF COTTON PROCESSING WASTES (Ref. 10)

Process	pH	Wastes (p.p.m.) BOD	Wastes (p.p.m.) Total Solids	Gallons Waste per 1,000 lbs. Goods	Pounds BOD per 1,000 lbs. Goods	Pounds Total Solids per 1,000 lbs. Goods
Slashing, sizing yarn	7.0-9.5	620-2,500	8,500-22,600	60-940	0.5-5.0	47-67
Desizing	-	1,700-5,200	16,000-32,000	300-1,100	14.8-16.1	66-70
Kiering	10-13	680-2,900	7,600-17,400	310-1,700	1.5-17.5	19-47
Scouring	-	50-110	-	2,300-5,100	1.36-3.02	-
Bleaching (range)	8.5-9.6	90-1,700	2,300-14,000	300-14,900	5.0-14.8	38-290
Mercerizing	5.5-9.5	45-65	600-1,900	27,900-36,950	10.5-13.5	185-450
Dyeing:						
Aniline Black	-	40-55	600-1,200	15,000-23,000	5-10	100-200
Basic	6.0-7.5	100-200	500-800	18,000-36,000	15-50	150-250
Developed Colours	5-10	75-200	2,900-8,200	8,900-25,000	15-20	325-650
Direct	6.5-7.6	220-600	2,200-14,000	1,700-6,400	1.3-11.7	25-250
Naphthol	5-10	15-675	4,500-10,700	2,300-16,800	2-5	200-650
Sulfur	8-10	11-1,800	4,200-14,100	2,900-25,600	2-250	300-1,200
Vats	5-10	125-1,500	1,700-7,400	1,000-20,000	12-30	150-250

ENVIRONMENTAL MONITORING 7

7.1 BACKGROUND

7.1.1 Introduction

The simple detection of a pollutant in the environment does not provide sufficient information to allow a judgement on the hazard or other effects presented by this contaminant.

The hazard of a toxic material is directly related to its concentration and distribution in the environment. Therefore, any reported data must present a true reflection of these parameters.

Theoretically speaking, once a sample has arrived in an analytical laboratory, it can be both quantitatively and qualitatively analysed. Therefore, it is imperative that the sample arriving at the laboratory be truly representative of the environmental pollutant in both quality and quantity.

7.1.2 Sample Collection

Some aromatic amines and azo dyes show a potential for existence in both air and water. No standard methods specific to the collection of either of these materials was identified; however, general methods of sample collection which may be applicable to these compounds deserve some discussion.

The physical aspects of water sampling are a relatively simple matter. Normal procedure requires that a clean glass

unit be used to collect and transport the sample. The predominant constraint is that the collected sample is representative of the specific flow. This requires that the sampling location has not been selected in an area where a local high or low concentration exists.

For accuracy, a number of samples are taken at each location for cross-checking, this also serves to identify transient concentration fluctuations.

Sampling the air is usually a more troublesome and complicated procedure since generally, chemical concentrations are very low. These problems necessitate special techniques which will ensure that sufficient material has been collected to allow analysis.

One commonly used air sampling method is the "grab bag" technique. Here, a plastic bag is used to catch and contain a gaseous air sample. Related techniques use glass bottles, glass vials, syringes or glass tubes as the containment vessels.

In the usual situations, when the contaminant concentration is low, methods of collection are applied which concentrate the contaminant. This is achieved by drawing large volumes of air through an adsorbing medium such as activated charcoal, alumina or chalk. The operational principle is based on drawing the air sample through the adsorbing medium, where a proportion of the contaminants will be extracted and remain on the adsorbant. Upon transfer to the analytical lab, the sample can be desorbed and analyzed.

This method has advantages, but its application requires a degree of skill. The volume of air drawn must be accurate, and the adsorbing medium must selectively remove the contaminants of interest. Similarly, the adsorbant must not have

been saturated and begun to discharge sample, thus giving inaccurate readings. In the lab, measures must be taken to ensure that the sample removed for analyses is in fact representative of the sample adsorbed.

Other sampling methods are practiced, but they are for the most part, variations of the two described above.

7.1.3 Sample Transportation

Once a sample has been collected in the field, it is usually necessary to transport it some distance to the analytical laboratory. Since this may require some time, it is necessary to take precautions to ensure that the sample remains unchanged during shipment or while awaiting analysis. These changes may be physical ones such as desorption of sample from activated charcoal; or leakage from a vial may result in sample loss.

Chemical changes may also occur in the sample. These may be the result of interaction with the adsorbing medium or container. Or conversely, they may be the result of increased concentration of various species creating an enriched atmosphere for reaction. Failure to prevent chemical changes can result in data indicating the presence of a species which in fact did not exist in the sampling environment, and the reporting of a concentration value of the original contaminants which is lower than reality.

Methods for sample preservation are numerous, and are normally specific for the sample involved. The preservation method could involve such diverse processes as altering the pH of an aqueous solution, to refrigerating an air sample.

7.2 ANALYSIS

7.2.1 Field

There are no field analytical methods which are specifically designed to detect or quantify aromatic amines or azo dyes. However, there are general measurement methods which may be adaptable for this purpose, and consequently a brief review is provided.

Gas detector tubes are available for semi-quantitative determination of aromatic amines in air. Draeger supplies one such tube for aniline. A colorimetric reaction between aniline and furfural, a white reagent, produce a dianiline derivative of hydroxyglutacondialdehyde which is red. The measurement range is from 1 to 20 ppm of aniline. Ammonia interferes if its concentration exceeds 50 ppm. Gastec, another commercial manufacturer of gas detector tubes, also provides a tube for aniline. The colorimetric reaction between aniline and sodium dichromate produces chromic phosphate which is green in colour. The measurement range is from 2.5 to 30 ppm. The aniline derivatives, dimethylaniline, monoethylaniline and o-toluidine produce similar stains by themselves.

Another detection method which may be adaptable to aromatic amine vapor detection is the portable hydrocarbon analyzer. This instrument operates by drawing air samples through a combustion chamber. Any combustible material is registered through changes in the heat generated. By calibration, an estimate can be made of the concentration of many organic compounds.

It should be noted that since most aromatic amine compounds and azo dyes have very low vapor pressures, they would be expected to occur primarily in particulate matter. No field methods for analysis of particulate matter currently exist. Extracts of particulate matter collected by high volume

samplers or other similar collectors may be analysed in the laboratory by methods which are described in the following paragraphs.

Contaminated water supplies are more difficult to sample and analyze in the field and currently there does not appear to be a simple method for either qualitative or quantitative analysis in the field.

7.2.2 Laboratory

Two types of samples are usually encountered in the laboratory: air samples and water samples. Air samples of vapors are usually adsorbed on silica gel or gas Chrom S and must be desorbed with a suitable solvent (1, 2). Analysis is by gas chromatography. Water or air particulate samples are extracted and subjected to clean-up procedures before analysis by spectroscopic or chromatographic procedures. The applications of these methods to the analysis of aromatic amines and azo dyes is presented below.

Spectroscopic Methods

Spectroscopic methods are simple and relatively sensitive. The main disadvantage is that these methods are non-specific and hence subject to interferences from other amines and related chemical species. Aromatic amines can be diazotized, coupled and analyzed as diazo dyes colorimetrically. Aniline, 1-naphthylamine and benzidine were diazotized and coupled with 1-naphthol and analyzed colorimetrically at 0.1 ppm levels (3). Aniline in wastewaters was determined in the concentration range 0.02 to 1 mg/L photometrically at 413 nm as the Schiff base formed by the reaction of aniline with p-dimethylaminobenzaldehyde (4). Benzidine is determined colorimetrically at 0.2 µg/L by analysis of the oxidation product formed by the reaction of benzidine and Chloramine-T reagent. The main interferences encountered are from substituted benzidines. This method is very sensitive and is used by the U.S.-E.P.A.

for the determination of benzidine in waters and wastewaters(5).

Chromatographic Methods

Chromatographic methods include thin layer chromatography (TLC), gas chromatography (GC) and high pressure liquid chromtography (HPLC). The main advantages of chromatographic methods are: (1) the analytes are separated, therefore the problems of interferences are greatly reduced; (2) higher sensitivity with the use of gas chromatography and specific element detectors.

Thin Layer Chromatography (TLC)

TLC is a very simple fast method, very easy to use but suffers from a lack of sensitivity that is required for trace analysis. It is well suited for monitoring higher levels of amines in commercial processes and products(6). In the TLC procedure, the sample is applied on the TLC plate developed and the components visualized by UV or by the use of spray reagents. To increase the sensitivity of the resolved amines, fluorescent reagents or reagents capable of forming Schiff gases are incorporated in the spray reagents. The compounds formed from the reaction of the amines with these reagents are then more sensitive to detection by fluorimetry or photometrically.

A combined TLC/GC procedure was used to determine trace aromatic amines in dyestuff(7). The TLC detection limit for benzidine, α- and β-naphtylamines, 3,3'-dichlorobenzidine and 4-dimethylaminoazobenzene was 200 ppm. Benzidine was detected in direct azo dyes at 10 ppm levels(8). The use of p-dimethylaminocinnamaldehyde increased the sensitivity of detection of the following amines to TLC analysis:

Aniline, α- and β-naphthylamines (0.1 ppm), o-phenylenediamine (0.05 ppm), m-and p-phenylenediamine (0.2 ppm), benzidine (0.02 ppm), aminobiphenyl (0.07 ppm) (9, 10). Aniline was

also determined by use of fluorescamine reagent(11).

Gas Chromatography (GC)

The GC method is simple and sensitive. It is however more time consuming than the other methods. This disadvantage is however offset by the sensitivity of the method and the reduction of interferences. Benzidine, α- and β-naphthylamines, 3,3'-dichlorobenzidine and 4-dimethylaminozobenzene were analyzed in dyestuffs at 100 ppm levels using GC with a flame ionization detector (FID)(7). The sensitivity of the method could be considerably improved by concentrating the sample extracts(7). Aromatic amines in air were determined by adsorption on silica gel, desorption with ethanol and analysis by GC-FID(1). The amines analyzed and their detection limits were as follows: Aniline, N,N-dimethylaniline, o-toluidine and 2,4-xylidine (5 ppm), o- and p-anisidine (0.1 ppm) and p-nitroaniline (1 ppm). 3,3'-dichloro-4,4'-diaminodiphenylmethane (MOCA) in air was determined at 2 ppm levels by adsorption on Gas Chrom S, desorption with acetone and analysis by GC-FID(2).

In an effort to enhance the sensitivity of amines to electron capture detection (ECD) amines were derivatized to polyfluoramides and analyzed by ECD-GC(12). The method has not found general applicability probably due to increased analysis time and relatively insufficient sensitivity enhancement. The most promising GC procedure providing the highest sensitivity utilizes a nitrogen-selective detector(13). Industrial aromatic amines in fish were analyzed by this procedure at 1 ppb sensitivity. Benzidine, 3,3'-dichlorobenzidine, α- and β-naphthylamines, 3,4-dichloroaniline are a few of the amines analyzed by this procedure. The main advantages of this method are: (1) increased sensitivity and (2) reduction of interferences because only N-containing compounds respond to this mode of detection.

High Pressure Liquid Chromatography (HPLC)

HPLC is the newest of the chromatographic techniques and shows promise of becoming an important analytical technique in the analysis of aromatic amines and dyes(14, 16). A combination of HPLC and UV detection or fluorescent detection utilizes some of the procedures already developed for TLC procedures. Model studies have indicated that most aromatic amines were detectable at picomole quantities(17). Aniline and its metabolites were detected at nanomole qunatities using reverse phase chromatography(18). Azo and anthraquinone dyes were analyzed at ppb sensitivity by HPLC using UV detection (19). The main advantages of the method are: (1) shorter retention times than GC analysis hence shorter analysis time and, (2) comparable sensitivity to GC methods (19).

7.3 ENVIRONMENTAL LEVELS (Section added by MOE Staff)

While the basic analytical methodology has been well developed, there is a relative dearth of actual analytical data relating to environmental levels of aromatic amines.

Few references were found on ambient atmosphere levels of aromatic amines. Indications are that aniline and diphenylamine vapors may be encountered in the vicinity of chemical manufacturing plants at the ppb level(20). However, monitoring near a distillation unit found no traces of p-phenylenediamine, 2-aminodiphenyl, diphenylamine or 4-aminodiphenyl at the 0.5 ppb level after sampling for one to two hours(21).

An extensive tabulation of the frequency of organic compounds found in various types of water samples indicates that only aniline and diphenylamine were detected in two of several hundred samples of finished drinking water in the United States and Europe(22). However, several aromatic amines such as aniline and its chlorinated derivatives, diphenylamine and dibenzylamine could be detected in a number of industrial

effluents as well as a few river water samples. Benzidine could be detected in only two of several hundred samples of effluent, and river water(22). Similarly, while surface waters from Dutch agricultural areas contained no or only trace amounts of aromatic amine pesticides, significant amounts of free aniline and several of its halogenated derivatives could be detected in samples of Rhine delta waters(23). Maximum concentrations of several aromatic amines in the river Waal in the Netherlands(24) ranged from 0.7 µg/L for o-toluidine to 12.7 µg/L for chlorotoluidine. Up to 96 µg/L of aniline and several of its derivatives were detected in effluents of a dye manufacturing plant in the United States (25).

Several aromatic amines, including 1-naphthylamine were detected in fish collected near dye manufacturers on the Buffalo River near Buffalo, N.Y.(26). The level of 1-naphthylamine found was 10 ppb, 100 yards downstream of the plant.

Benzidine residues could be detected in several azo dyes, such as Direct Bordeau (17-35 ppm) and Direct Brown KKh (38 ppm), while no free benzidine could be detected in Direct Black 3, with a sensitivity of less than 10 ppm(27). Up to 3 per cent of 4-aminobiphenyl, a potent bladder carcinogen in man, could be detected in commercial samples of 2-aminobiphenyl, a common analytical reagent(28).

Specific analytical data are lacking with regard to ambient environmental levels of aromatic amines and azo dyes in Ontario.

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APPENDIX I

DISPERSION OF TIRE RUBBER IN THE ENVIRONMENT

Tires provide the sole contact between a vehicle and the roadway surface and consequently must transmit the interactive forces required for propulsion and control.

In doing this, tread material is worn away by a variety of processes ranging from simple abrasion to high temperature pyrolysis.

It is estimated that the average wear rate per tire is 90 mg/km, with an estimated 5-20 mg/km during cruise driving and 500 mg/km in moderate cornering.(1)

In one study, it is reported that from 2% to 10% of airborne dust near a freeway was airborne tire tread rubber.(2)

During normal driving conditions, hydrocarbons and sulfur gases are emitted continuously. The individual hydrocarbons identified include styrene, butadiene, isoprene and vinyl cyclohexene.(3) This suggests that the gases are formed from the degradation of tread polymer by high temperature pyrolysis.

Measured particulates from tire wear range in size from 0.01 μm to more than 30 μm, with the larger particles dominating the total mass.(3)

Measurements near a California freeway showed that most of the rubber debris had settled within a 5m strip of the pavement edge. The rubber distribution is not even over this strip, but best fits an exponentially decreasing concentration curve moving away from the pavement edge.(3) This would seem to confirm the contention that most wear particles are not air suspendable.(3)

The overall concentration of rubber in the soil beside the freeway was found to be low. It has been speculated that chemical degradation is a contributing factor in the removal of rubber from the environment.(3) This is consistent with the observation that pyrolysis processes cause the vapourization of tire components. With the removal of anti-oxidants by this process, it seems clear that the rubber particles would be highly susceptible to degradation. Similarly, the settled dusts would be highly susceptible to biodegradation.

The reported analytical data has not addressed the question of distribution and dissipation of heavy metals, such as cadmium, which are an integral part of the tire tread. This is obviously a question which should be investigated.

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APPENDIX II

STANDARDS AND CRITERIA

Information specific to ambient concentrations of either aromatic amines or azo dyes is not currently available. This appears to be as a result of the general order of investigative priorities in which these compounds stand relatively low.

As a consequence, standards limiting environmental concentrations of either amines or azo dyes are not common. As of 1974(1), seven countries had ambient air quality standards for aniline. These are detailed in Table A.2.1.

TABLE A.2.1.

AMBIENT AIR QUALITY STANDARDS FOR ANILINE

Country	Level In mg/m^3	Level In ppm	Averaging Period
Bulgaria	0.03	0.008	24 h
	0.05	0.013	20 min
Czechoslovakia	0.03	0.008	24 h
	0.05	0.013	30 min
Federal Republic of German	0.8	0.2	30 min
	2.4[1]	0.6[1]	30 min
German Domocratic Republic	0.03	0.008	24 h
	0.05	0.013	30 min
Roumania	0.02	0.005	24 h
	0.05	0.013	30 min
U.S.S.R.	0.03	0.008	24 h
	0.05	0.013	30 min
Yugoslavia	0.03	0.008	24 h
	0.05	0.013	30 min

[1] This is a short-term exposure limit (i.e. 30 min.) not to be exceeded more than once in every four hours.

Further environmental standards are embodied in the Union of Soviet Socialist Republic's and Poland's health protection or width of protection zones.

Implicit in the establishment of these zones is the recognition of the potential hazard these industries may present to surrounding residents. Residences are not allowed in these zones as a method of preventing significant human exposure to potentially hazardous airborne pollutants.

Excerpts from Reference 1 are shown below, for industries that are involved in the production or handling of aromatic amines in the U.S.S.R.

TABLE A.2.2.

U.S.S.R. HEALTH PROTECTION ZONES

Class I: Health Protection Zone 1000 m Wide.

Production of intermediate products of the aniline dye industry in the benzene and ether series (aniline derivatives, nitrobenzene, alkyl amines, phenol, etc.) where total output is over 1000 tons per year.

Class II: Health Protection Zone 500 m Wide.

Production of intermediate products of the aniline dye industry in the benzene and ether series (aniline derivatives, nitrobenzene, alkyl amines, phenol, etc.) where total output is under 1000 tons per year.

Production of vat dyes from all types of azotol and azo amines.

Experimental plants in the aniline dye industry with a total capacity of 2000 tons per year and an output of under 1000 tons per year.

TABLE A.2.3.

POLISH WIDTH OF PROTECTION ZONES

Class A: Width of Protection Zone 1000 m.

Production of prefabricates in aniline dye industry of ether and benzene series: industrial plant capacity above 1000 tons per year.

Class B: Width of Protection Zone 500 m.

Production of prefabricates in aniline dye industry of benzene series; industrial plant of general production capacity below 1000 tons per year.

Production of azo and azo amine dyes.

A considerable body of information regarding occupational exposure to aromatic amines does exist, and some industrialized countries have adopted maximum concentration limits (2,3,4).

These limits are based on the belief that these compounds present a real and distinct hazard to the worker.

The following table, Table A.2.4., details various occupational exposure standards.

TABLE A.2.4.

OCCUPATIONAL EXPOSURE STANDARDS

	Aniline (Skin Exposure)	Benzidine	Naphthylamine	Methylene dianiline	Phenylene-diamine (Skin Exposure)
Australia	5 ppm	carcinogen	carcinogen	-	0.1 mg/m^3
Federal Republic of Germany	5 ppm	carcinogen	carcinogen	-	0.1 mg/m^3
Finland	5 ppm	carcinogen	carcinogen	-	0.1 mg/m^3
Canada (Ontario)	2 ppm	carcinogen	carcinogen	0.04 mg/m^3	0.1 mg/m^3
USA (ACGIH)	2 ppm	carcinogen	carcinogen	-	0.1 mg/m^3
USA (OSHA)	5 ppm	carcinogen	carcinogen	10 ppm	0.1 mg/m^3

Direct comparison between exposure values should be made with caution. There is presently no consensus between industrialized countries as to what basis should be used when considering exposure limitations. Therefore, even though the numerical value for exposure in two countries may be identical, the working conditions may be sufficiently different to make a direct comparison invalid. As an example, one country may commonly require a twelve hour work day, while another required only eight. Similarly, one country may establish a limit at which absolutely no response is observable in the worker, while another country may find minor irritation acceptable.

Corresponding values for ambient or occupational exposure to azo dyes have not been uncovered.

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3. United States Department of Labour, Occupational Safety and Health Administration, Personal Communication, May 9, 1979.

4. Occupational Exposure Limites for Airborne Toxic Substances; International Labour Office, Geneva, 1977.

APPENDIX III

FATE OF 3,3'-DICHLOROBENZIDINE IN AQUATIC ENVIRONMENTS

This section is a summary of the report on this subject authored by Sikka and associates and published by the USEPA in 1978.(1)

3,3'-Dichlorobenzidine (DCB) is widely used as an intermediate in the manufacture of azo pigments. It is of considerable commercial importance; total DCB production in the United States in 1972 was about 4.6 million pounds.

With current work practices, effluents containing this chemical are discharged directly into receiving waters. Moreover, the discharge of dichlorobenzidine-pigment wastes into receiving waters constitutes an additional source of DCB contamination in the environment since free, unreacted DCB is reported to be present in these pigments.

Dichlorobenzidine is known to induce cancer in animals and is regarded by the Occupational Health and Safety Administration (OSHA) as being carcinogenic to man.

DCB and its metabolites accumulate in fish and could pose a health hazard if fish from contaminated waters were to be used as human food.

The potential hazard of DCB may be compounded by its biological or non-biological conversion to compounds of even greater toxicity and/or persistence than the parent chemical. For instance, it is believed that in the case of carcinogenic aromatic amines, it is the metabolites of the chemicals that produce the carcinogenic response. Furthermore, potential degradation products of DCB, such as benzidine, may constitute an even greater carcinogenic hazard.

A number of physical, chemical and biological factors determine the fate of a chemical in the aquatic environment. These include hydrolysis, photodegradation, microbial degradation, and uptake and metabolism by aquatic organisms. Currently nothing is known about the effect of these factors on the persistence and transformation of DCB in the aquatic environment.

This study was undertaken to assess the role of some of the processes that may determine the environmental behavior of the chemical.

In the study section examining the disappearance of DCB in natural waters, it was noted that greater than 95% of the sample DCB was adsorbed onto natural pond and lake sediments. Only a portion of the adsorbed DCB could be recovered from the sediment after a time, leading the authors to suggest that it was reacting with sediment constituents.

When exposed to either natural or artifical light in aqueous solution, DCB was rapidly dechlorinated sequentially to monochlorobenzidine and then benzidine. The half life for the initial reaction was in the order of 90 seconds.

This reaction is significant in that in the degradation process, products of either equal or greater toxicity are produced.

When exposed to naturally occurring aquatic micro-organisms, DCB was reported as being essentially non-biodegradable. When incubated with micro-organisms for a three week period, chemical losses were reported to be negligible. A similar result was reported for activated sludge. No evidence was seen to indicate that sludge micro-organisms can be induced to metabolize DCB.

Dichlorobenzidine was rapidly bioconcentrated in bluegill sunfish, with mortality occurring prior to establishment of a chemical equilibrium between water and fish. Bioconcentration factors of 132-554 were achieved at this point. The only metabolite detected in the fish was an acid-labile conjugate of DCB.

The ability of DCB to concentrate in aquatic organisms may pose a direct hazard to human health through consumption of contaminated fish.

In summary, evidence suggests that DCB is a non-biodgradable, toxic material. It is dangerous to fish and humans, both as the initial compound and its most prevalent degradation products.

REFERENCES

1. Sikka, C.H., et al; "Fate of 3,3'-Dichlorobenzidine in Aquatic Environments", USEPA, EPA-600/3-78-068; Athens, Georgia, 1978.

eight compounds is negative to the present, in the majority of cases the testing has not been adequate to rule out possible carcinogenic effects.

Closure

The International Agency for Research on Cancer has recently issued a Supplement to its Monographs, Volumes 1 to 20, (September 1979), in which the experimental evidence of carcinogenicity for the chemicals reviewed in their monographs is evaluated with respect to the potential carcinogenic risk which these chemicals may present to humans. This Supplement should be consulted when the carcinogenic risk to humans of a specific chemical compound is being assessed.

APPENDIX IV

SUMMARY OF RELEVANT IARC CARCINOGENICITY ASSESSMENTS

Aromatic Amines

Data relating to the carcinogenicity of 32 aromatic amines have been reviewed by the International Agency for Research on Cancer, Vol. 16, 1978.

Of eight examined aromatic amines used as hair dyes, three (meta-phenylenediamine, para-phenylenediamine and 2,4-diaminotoluene) were discussed in the body of this report. In the case of 1,2-diamino-4-nitrobenzene and 1,4-diamino-2-nitrobenzene, the evidence as to their carcinogenicity in animals is equivocal. For three others, namely 4-amino-2-nitrophenol, 2,4-diaminoanisole and 2,5-diaminotoluene, the evidence to date suggests that they are non-carcinogenic.

Of nine aromatic amines which have been used as colouring agents, all but one are considered carcinogenic on the evidence from animal experiments. These are:

Benzyl Violet 4B
Vlue VRS
Brilliant Blue FCF Diammonium and Disodium Salts
Fast Green FCF
Guinea Green B
Light Green SF
Rhodamine B
Rhodamine 6G

In the case of Acridine Orange, the evidence is equivocal.

Of fifteen aromatic amines used as industrial chemicals, there is evidence that five were carcinogenic in animals. These were:

N,N-diacetyl benzidine
3,3-dichloro-4,4-diaminodiphenyl ether

5-nitroacenaphthene
N-phenyl-2-naphthylamine
4,4-thiodianiline

For 9 other amines the data were either inadequate for proper evaluation or the results were equivocal. These were:

5-aminocenaphthene
anthranilic acid
para-chloro-ortho-toluidine
cinnamyl anthranilate
4,4-diaminodiphenyl ether
2,4-diphenyldiamine
ortho-toluidine
2,4-xylidine
2,5-xylidine

One amine, para-aminobenzoic acid, was found not carcinogenic though the data were too limited for proper evaluation.

Aromatic Azo Compounds

The evidence as to the carcinogenicity of 32 aromatic azo compounds was examined by the International Agency for Research on Cancer, Vol. 8, 1975. Evaluation of the data was difficult because of uncertainty as to the exact composition of the materials used in the animal experiments, and because of the inadequate design of many of the earlier studies. Despite extensive searches, no published evidence was found to show whether the aromatic azo compounds considered were carcinogenic to man.

Of the 32 aromatic azo compounds examined, the following 11 were considered carcinogenic on the evidence from aminal studies:

para-aminoazobenzene
ortho-aminoazobenzene
Chrysodine

Citrus Red No. 2
para-dimethylaminoazobenzene
Evans Blue
Oil Orange SS
Ponceau MX

For thirteen aromatic azo compounds the animal evidence as to their carcinogenicity was equivocal. These compounds were:

Amaranth
azobenzene
C.I. Disperse Yellow 3
diacetylaminoazobenzene
2,6-diamino-3-(pheylazo)-pyridine
para-dimethylaminobenzenediazo sodium sulphonate
4-hydroxyazobenzene
Methyl Red
Orange I
Scarlet Red
Sudan II
Sudan III
Yellow OB

In the case of eight aromatic azo compounds the animal evidence for their carcinogenicity was essentially negative to date. These were:

Carmoisine
D and C Red No. 9
Orange G
Ponceau SX
Sudan Brown PR
Sudan Red 7B
Sunset Yellow FCF
Yellow AB

It should be emphasized that while the evidence for these